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Covalent Tetrahydroborates

K.N.Semenenko, O.V.Kravchenko, and V.B.Polyakova

The properties, structure, and methods of preparation of the tetrahydroborates of beryllium, aluminium, and certain heavy metals (zirconium, hafnium, thorium, and uranium) are reviewed.
These compounds, which can provisionally be grouped together as the so-called covalent complex hydroborates, have much in common both as regards physical properties and high reactivity and as regards the nature of the chemical bond and the character of the chemical changes in which the $M(BH_4)_n$ molecules participate. The main types of chemical reactions of the covalent tetrahydroborates, the structural principles lying at the basis of their molecular and crystal structures, and also the possibility of using covalent tetrahydroborates in various fields of inorganic synthesis are examined. 114 references.

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I. INTRODUCTION

For the last 15—20 years the saltlike alkali metal tetrahydroborates, the crystal lattices of which contain isolated tetrahedral BH_4^- ions, have been the subject of an intensive investigation, which has shown the possibility of their use in preparative inorganic chemistry and chemical technology.

Considerably less attention has been paid to the tetrahydroborates of metals, the "cations" of which show high reduced moments z/r (beryllium, aluminium, and the heavy metals zirconium, hafnium, thorium, and uranium), where z is the charge and r the radius of the ion.

Evidently, the main reason for ignoring the experimental chemistry of the complex covalent tetrahydroborates of the $M(BH_4)_n$ type was the difficulties associated with the preparation and investigation of these extremely reactive and volatile compounds.

Actually, aluminium tetrahydroborate $Al(BH_4)_3$, for example, reacts explosively in the solid, liquid, and gaseous states with atmospheric oxygen and moisture, beryllium tetrahydroborate $Be(BH_4)_2$ and uranium tetrahydroborate $U(BH_4)_4$ are spontaneously inflammable in air, and so forth.

The relatively low thermal stability of the covalent tetrahydroborates (they all decompose rapidly and irreversibly in the range 130—150°C) gives rise to additional difficulties in their preparation.

Nevertheless the chemistry of the complex covalent hydroborates is much richer and more interesting than that of the saltlike tetrahydroborates. The $M(BH_4)_n$ molecules exhibit a dual reactivity: the BH_4 group in them is simultaneously a carrier of the functions of both a tetrahedral BH_4^- "ion" and an H_2BH_2 bridging group, close in structure and properties to the H_2BH_2 group in the diborane molecule.

The saltlike nature of the tetrahydroborates $M(BH_4)_n$ increases in the sequence:

	$Be(BH_4)_2$	$Al(BH_4)_3$	$U(BH_4)_4$	$Zr(Hf)(BH_4)_4$	$U(BH_4)_3$	$Ca(BH_4)_2$
z/r	4.4	4.3	3.8	3.7	2.8	2.0

It is interesting to trace how the structure of the BH_4 group situated in the field of the "cation" M and the type of the M—H—B chemical bond vary as the reduced moment z/r is increased.

In the most saltlike tetrahydroborate (that of U^{III}) the proper symmetry of the BH_4 group is evidently the same as in the tetrahydroborates of univalent cations, T_d. On going to molecular structures with $z/r > 3$ the nature of the bonding of the BH_4 group with the cation is more complicated. In the M^{IV} tetrahydroborates the symmetry of the BH_4 group is decreased to C_{3v} and a new type of multicentre bridging bond MH_3B, unknown in the chemistry of the boron hydrides, is formed.

The $Al(BH_4)_3$ molecule contains AlH_2B bridges close in structure to the BH_2B fragments in the B_2H_6 molecule (symmetry of the BH_4 group C_{2v}) and from the nature of the chemical bond in it is a complete analogue of diborane.

The $Be(BH_4)_2$ molecule, the structure of which is considered in detail on p. 5, can be described as the result of "association" of a distorted B_2H_6 molecule and a BeH_2 molecule[1] or as a combination of two BH_4 tetrahedra with a common vertex and a planar BeH_3 group, which complete a six-membered ring $\{BeH_3B_2\}$.[2]

The dual reactivity of the tetrahydroborates $M(BH_4)_n$ connected with the intermediate nature of the bond between the BH_4 group and the M atoms, appears clearly in the chemistry of aluminium tetrahydroborate, which reacts with alkenes like diborane and with ammonia like the tetrahydroborate $[Al(NH_3)_6](BH_4)_3$.[3,4]

Since the covalent tetrahydroborates, like diborane, are electron-deficient compounds—the number of atomic orbitals in the $M(BH_4)_n$ molecules is greater than the number of valency electrons—a specific type of reaction, not characteristic of the saltlike tetrahydroborates, is inherent for them. This refers to the addition of molecules which are donors of electrons, with the formation of new molecular structures of the type $M(BH_4)_n.mL$ (I) or $[M(BH_4)_nX]^-$ (II), in which the atom M, which exhibits a coordination number anomalously high from the viewpoint of classical ideas, is at the centre of a coordination polyhedron with an unusual configuration.

Examples of such compounds are the complexes[4,5] of aluminium tetrahydroborate with trimethylamine, trimethylphosphine, and trimethylarsine, in the molecules of which the aluminium atom is surrounded by three boron atoms, six hydrogen atoms, and a nitrogen atom, situated at the vertices of greatly distorted $[H---AlH_5---N]$ pentagonal bipyramids.

The structures of compounds of types (I) and (II) are of exceptional interest in connection with the definition of the concepts of "valency" and "coordination" number, the classical treatment of which is inapplicable for the description of most light metal hydrides.

The prospects of the practical use of the tetrahydroborates $M(BH_4)_n$ is evidently linked with their use as starting materials in the preparation of new inorganic compounds containing an M—H—B bond and also with their high volatility and with the possibility of their use in this connection for separating elements with very similar properties, for example, Zr and Hf or the isotopes ^{235}U and ^{238}U.[6-10]

It has also been noted repeatedly[7,8] that the light metal tetrahydroborates, which have high heats of combustion, can be regarded as promising components of rocket fuels.

II. METHODS OF SYNTHESIS

1. DOUBLE DECOMPOSITION BETWEEN METAL HALIDES AND ALKALI METAL AND ALUMINIUM TETRAHYDROBORATES

Schlesinger[11,12] was the first to use the method of double decomposition for obtaining aluminium and beryllium tetrahydroborates from the corresponding chlorides and alkali metal tetrahydroborates by the reactions:

$$BeCl_2 + 2\,LiBH_4 \xrightarrow{140^\circ} Be(BH_4)_2 + 2\,LiCl\ , \quad (1)$$

$$AlCl_3 + 3MBH_4 \xrightarrow{100-130^\circ} Al(BH_4)_3 + 3\,MCl\ . \quad (2)$$

Reactions (1) and (2) take place in the solid phase at 100—130°C, the yield of the desired product depending on the ratio of the reagents and the nature of the tetrahydroborate used. It has been shown[12,13] that the greatest yield of aluminium and beryllium tetrahydroborates (90—95%) occurs when the metal chlorides react with lithium tetrahydroborate in ratios close to stoichiometric. When sodium tetrahydroborate is used the yield is considerably less (~50%), but the yield of aluminium tetrahydroborate can be increased by the introduction of a large excess of the metal chloride into the reaction mass[11,12]. When potassium tetrahydroborate is used, the yield of aluminium and beryllium tetrahydroborates by reactions (1) and (2) are reduced almost to zero.

However, when potassium tetrahydroborates reacts with aluminium chloride in the presence of lithium chloride the yield of aluminium tetrahydroborate is increased to 40—50%.[14] In addition to the main products from reactions (1) and (2), side-products are formed: diborane, hydrogen, and chloro-substituted derivatives of tetrahydroborates of composition $MCl_x(BH_4)_{n-x}$.[11,15]

Reaction (2) can also be effected in the presence of inert organic substances: petroleum, mineral oil, heavy mineral oil with graphite flakes, benzene; this facilitates the charging of the reagents, the mixing of the reaction mass, and the discharge of the product[16-20].

Lithium tetrahydroborate reacts with zirconium(IV) chloride in a manner similar to reactions (1) and (2):

$$ZrCl_4 + 4\,LiBH_4 \rightarrow Zr(BH_4)_4 + 4\,LiCl\ . \quad (3)$$

The yield of zirconium tetrahydroborate by reaction (3) is 77%; when sodium or potassium tetrahydroborate replaced the lithium salt zirconium tetrahydroborate could not be obtained by this method[21].

For uranium tetrahydroborate the "dry" method of synthesis—heating mixtures of alkali metal tetrahydroborates with uranium(IV) fluoride up to 200°C—did not give results. Uranium and thorium tetrahydroborates were obtained by the reaction of uranium(IV) and thorium(IV) fluorides with aluminium tetrahydroborate[22-24]:

$$MF_4 + 2\,Al(BH_4)_3 \rightarrow 2\,AlF_2BH_4 + M(BH_4)_4\ . \quad (4)$$

When there is an excess of aluminium tetrahydroborate the yield of uranium tetrahydroborate reaches 80%.[22,23] The method can also be used for the preparation of zirconium tetrahydroborate:

$$ZrCl_4 + 2Al(BH_4)_3 \rightarrow 2\,AlCl_2BH_4 + Zr(BH_4)_4\ . \quad (5)$$

However, in this instance there are additional difficulties associated with the separation of the reaction products, the volatilities of which are very similar. Zirconium and hafnium tetrahydroborates can be obtained from aluminium tetrahydroborate and fluoro-complexes[24,25]:

$$NaMF_5 + 2Al(BH_4)_3 \rightarrow NaF + 2AlF_2BH_4 + M(BH_4)_4\ . \quad (6)$$

Fluoro-complexes are used because zirconium(IV) and hafnium(IV) fluorides do not react directly with aluminium tetrahydroborates[26].

2. REACTION OF METAL ALKYLS OR METAL HYDRIDES WITH DIBORANE

The first covalent tetrahydroborate obtained by the reaction of a metal alkyl with diborane was that of aluminium[27,28]:

$$Al(CH_3)_3 + 2B_2H_6 \rightarrow Al(BH_4)_3 + B(CH_3)_3 . \quad (7)$$

The yield of the reaction was 70—80%. This method is also applicable for the preparation of beryllium tetrahydroborate[29].

Reaction (7) is inconvenient preparatively since it is slow, with the formation of intermediate products of the $Al(BH_4)_x(CH_3)_{3-x}$ type, which are difficult to separate.

Beryllium tetrahydroborate can also be obtained by the action of diborane on beryllium hydride[30]. There is a report of the possibility of obtaining aluminium tetrahydroborate in yields of up to 90% by the action of diborane on crystalline lithium tetrahydroaluminate at 70—80°C:[31]

$$LiAlH_4 + 2B_2H_6 \rightarrow LiBH_4 + Al(BH_4)_3 . \quad (8)$$

3. PREPARATION IN THE PRESENCE OF SOLVATING SOLVENTS

Fuchs and Kollonitsch[32,33] described the preparation of aluminium tetrahydroborate from calcium tetrahydroborate and aluminium chloride in tetrahydrofuran (THF) solution:

$$3Ca(BH_4)_2 + 2AlCl_3 \cdot C_4H_8O \xrightarrow{C_4H_8O} 3CaCl_2 + 2Al(BH_4)_3 \cdot C_4H_8O . \quad (9)$$

When the solution is cooled to −60°C a complex of aluminium tetrahydroborate and tetrahydrofuran crystallises from it.

Complexes of aluminium tetrahydroborate with diethyl ether are formed by the reactions[31,34]:

$$4AlH_3 \cdot Et_2O + 3BCl_3 \xrightarrow{Et_2O} Al(BH_4)_3 \cdot Et_2O + 3AlCl_3 \cdot Et_2O , \quad (10)$$

$$3LiAlH_4 + 3BCl_3 \xrightarrow{Et_2O} Al(BH_4)_3 \cdot Et_2O + LiCl + 2AlCl_3 \cdot Et_2O , \quad (11)$$

$$2AlH_3 \cdot Et_2O + nB_2H_6 \xrightarrow{Et_2O} 2H_{3-2n}Al(BH_4)_{2n} \cdot Et_2O . \quad (12)$$

The reaction of uranium(IV) fluoride with lithium tetrahydroborate in diethyl ether gives a complex of uranium tetrahydroborate with the ligand-solvent[22]. It is noteworthy, however, that the oxonium complexes of the covalent tetrahydroborates are stable compounds from which the non-solvated tetrahydroborates cannot be separated.

The methods of synthesis considered in sections II. 2 and II. 3 are preparatively inconvenient or associated with the impossibility of using difficulty available and costly initial substances. The most promising methods of preparation of the covalent tetrahydroborates are those based on double decomposition between metal halides and alkali metal or aluminium tetrahydroborates.

III. PHYSICOCHEMICAL PROPERTIES AND REACTIVITY

Under normal conditions the covalent tetrahydroborates $M(BH_4)_n$ are crystalline, except for aluminium tetrahydroborate, which is a colourless, mobile, low-boiling liquid.

Table 1 gives some physicochemical properties of the tetrahydroborates $M(BH_4)_n$.

In addition, the following quantities have been determined for liquid aluminium tetrahydroborate[35-37]: (a) coefficient of viscosity 2.0 mP (25°C); (b) free energy of formation ΔG_i° 36.2 kcal mole^{-1}; (c) specific heat capacity C_p° = 46.8 cal deg^{-1} mole^{-1}; (d) entropy of vaporisation ΔS_e = 22.6 e.u.

Table 1. Physicochemical properties of the covalent tetrahydroborates.

Compound	M.p., °C	B.p., °C	Coefficients A and B in the equation $\lg P = A - B/T$	ΔH_f (1) ΔH_e^f (2)	ΔH_{rev}	Density, g cm^{-3}
$Al(BH_4)_3$	−64.5[28]	44.5[28]	A B 7.808 1565[35] 9.56796 1789.1[36]	1.68[27] (1) 7.2 (2)	−72.1[37] −26.4[38] −74.7[7]	0.544 (20°)[28] 0.7866— 0.0007937[36]
$Be(BH_4)_2$		91.3 sublimation temp. (Ref.29)	11.772 3240[29]	14.81 (2)[29]	−25.8[7]	9.604 (20°)[7]
$U(BH_4)_4$	decompn. temp. >70[22]	—	13.65 4265[22]	—	—	—
$Zr(BH_4)_4$	29.7[24]	123 extrapolated	10.919 2983[24]	4 (1) 9.3 (2)[25]	—	1.13 (20°) 1.01 (30°)[39]
$Hf(BH_4)_4$	29[24]	118[24]	10.719 2983[24]	3 (1) 9.7 (2)[24]		1.85 (20°) 1.60 (30°)[39]
$Th(BH_4)_4$[24]	203 with decomposition	—	P=0.05 mmHg at 130° P=0.20 mmHg at 150°	—	—	—

As Table 1 shows, there has not yet been any serious investigation of the thermodynamic characteristics of covalent tetrahydroborates except for the melting and boiling points. For example, several values have been given for the heats of formation of aluminium tetrahydroborate, the reliability of these being equally doubtful. The difficulties in the determination of the thermodynamic characteristics of covalent tetrahydroborates are connected with their extremely high reactivity. For aluminium tetrahydroborate, for example, it is almost impossible to select an oxidant with which this compound will not react explosively during simple mixing under normal conditions.

Beryllium, aluminium, zirconium, hafnium, and uranium tetrahydroborates are less stable thermally than saltlike tetrahydroborates of univalent cations. Aluminium tetrahydroborate decomposes even at room temperature, with the formation of hydrogen. The decomposition is faster in the gas phase than in the liquid. Certain substances, for example, alloys of aluminium and copper, catalyse the decomposition[40]. Solutions of aluminium tetrahydroborate in saturated hydrocarbons with up to 50% $Al(BH_4)_3$ decompose at the same rate as the pure substance[41].

According to Schlesinger[11,42], aluminium tetrahydroborate is stabilised during prolonged storage under normal conditions or when heated for several days at 40°C. It is suggested that the stabilisation is linked with the formation of decomposition products which are inhibitors of further decomposition reactions.

The NMR spectrum of aluminium tetrahydroborate that has been kept for some time at 80°C differs from the spectra of "ordinary" aluminium tetrahydroborate[43]. The artificial introduction of diborane reduced the difference in the spectra, which suggested a reversible change by the following mechanism:

$$2\,Al(BH_4)_3 \rightleftarrows Al_2H_2(BH_4)_4 + B_2H_6\ . \qquad (13)$$

The probable mechanism of deuterium exchange between deuteriated diborane and aluminium tetrahydroborate[44] agrees with this assumption. However, the existence of $Al_2H_2(BH_4)_4$ in the gas phase is not confirmed by investigations of the infrared spectra[44].

Raising the temperature facilitates the more rapid decomposition of $Al(BH_4)_3$, with release of hydrogen and formation of a mixture of a crystalline powder and an amorphous black substance, which reacts with water with the release of hydrogen[45,46].

Beryllium tetrahydroborate is stable at room temperature and starts to decompose at 123°C.

The rate of decomposition of uranium and zirconium tetrahydroborates at room temperature is low; these substances are completely stable at 50–60°C. Further heating greatly increases the rate of pyrolysis. Uranium(IV) tetrahydroborate decomposes at 100°C with the formation of a red-brown uranium(III) tetrahydroborate[22]:

$$2\,U(BH_4)_4 \xrightarrow{100^\circ} 2\,U(BH_4)_3 + B_2H_6 = H_2\ . \qquad (14)$$

The decomposition of $U(BH_4)_4$ at 150°C leads to the formation of a metallic mirror on the walls of the pyrolyser and the release of hydrogen. Unlike uranium(IV) tetrahydroborate, uranium(III) tetrahydroborate is pyrophoric and decomposes explosively when heated. The decomposition of $U(BH_4)_4$ proceeds mainly in the gas phase and is accelerated in the presence of Hg, Cu, Ni, and "Pyrex" glass[22].

Zirconium and hafnium tetrahydroborates start to decompose at an appreciable rate when heated to 60–70°C.[24] Thorium tetrahydroborate decomposes slowly at 150°C and rapidly at 300°C. Its pyrolysis at 300°C leads to the formation of a metallic mirror of composition ThB_4, together with hydrogen[24].

The high reactivity of covalent tetrahydroborates in relation to oxygen and to compounds which contain positively polarised hydrogen atoms is due to the low strength of the MH_nB bridging bonds in the $M(BH_4)_n$ molecules, the unsaturated nature of these compounds, and their high heats of combustion or hydrolysis. Actually, all the covalent tetrahydroborates react with water even at ~–80°C.[47] The products of the reaction are the hydroxides of the corresponding metals, boric acid, and hydrogen. The hydrolysis of aluminium tetrahydroborate, like, probably, that of other tetrahydroborates, proceeds in stages, with the formation in the first stage of diborane, which is subsequently hydrolysed to hydrogen and boric acid[47,48]:

$$Al(BH_4)_3 + 3H_2O \rightarrow Al(OH)_3 + {}^3/_2B_2H_6 + 3H_2\ , \qquad (15)$$

$${}^3/_2\,B_2H_6 + 9\,H_2O \rightarrow B(OH)_3 + 9H_2\ . \qquad (16)$$

At room temperature aluminium and beryllium tetrahydroborates react explosively with water. However, in the hydrolysis only 70–80% of the theoretically necessary hydrogen is released and solid yellow–brown polymeric substances are formed[47].

The presence of traces of water (which is a catalyst of the oxidation) is necessary for the spontaneous ignition of mixtures of covalent tetrahydroborates and oxygen[24,29,50]. For example, uranium tetrahydroborate $U(BH_4)_4$ is only slowly oxidised in dry air, whereas all the covalent tetrahydroborates are spontaneously combustible in air[31,49–51].

The tetrahydroborates $M(BH_4)_n$ react with hydrogen chloride at –80°C with the formation of the chlorides of the corresponding metals, diborane, and hydrogen[24,28]. The main side-reaction here is the formation of halogen-substituted boron hydrides, for example:

$$B_2H_6 + HCl \rightarrow B_2H_5Cl + H_2\ . \qquad (17)$$

IV. STRUCTURE

The most effective method of studying the structure of the molecules of the volatile covalent tetrahydroborates $M(BH_4)_n$ was gas electron diffraction.

Bauer and Beach[52] made the first studies in this field. They found the $Al(BH_4)_3$ molecule to have the configuration of a trigonal prism with an equilateral triangle of B atoms in the equatorial plane. The Al atom is situated at the centre of the triangle and the H atoms of the AlH_2B bridging bonds at the vertices of the trigonal prism.

In principle, the electron diffraction results also do not contradict the other possible model (octahedral)[53,54], which differs from that considered above in the angle of slope of the plane of the AlH_2B bonds to the plane of the AlB_3 triangle: in the prismatic model this angle is 90°, in the octahedral 45°. The symmetry element σ_h is absent from the octahedral model. The choice between the two possible configurations was made on the basis of a detailed investigation of the infrared and Raman spectra of gaseous[55,56] and liquid[57] $Al(BH_4)_3$ and its isotope-substituted analogues $Al(^{11}BD_4)_3$, $Al(^{10}BH_4)_3$, and $Al(^{10}BD_4)_3$. As Table 2 shows, for the D_{3h} prismatic model of the $Al(BH_4)_3$ molecule there should be 13 absorption bands in the infrared spectrum and 5 polarised and 14 non-polarised bands in the Raman spectrum. For the D_3 octahedral model there should be 21 absorption bands in the infrared spectrum and 7 polarised and 14 non-polarised bands in the Raman spectrum. The experimental results agree better with the prismatic model (see Table 2).

Almeningen and coworkers[58] further refined the interatomic distances and valence angles in the prismatic model of $Al(BH_4)_3$. The model of the $Al(BH_4)_3$ molecule according to Almeningen is given in Fig. 1.

The NMR spectra of aluminium tetrahydroborate were investigated in 1955 [43] and in 1967.[59].

In the 1967 analysis of the NMR spectra of various specimens of $Al(BH_4)_3$ [59] the possibility of the molecular polymorphism of $Al(BH_4)_3$ was suggested, linked with the reversible conversion of the prismatic molecule into the octahedral, which hypothetically exists in the liquid phase or in benzene solution. This hypothesis is based on the fact that the structure of the NMR spectra characteristic for a BH_4 group with four equivalent protons appears for specimens of $Al(BH_4)_3$ which have undergone different preliminary treatments and are in different states of aggregation at different temperatures. However, our results[60] do not agree with hypothesis of the molecular polymorphism of aluminium tetrahydroborate.

We showed that the infrared spectra of crystalline $Al(BH_4)_3$ are almost constant in the temperature range from –75° to –90°C and identical with the infrared spectrum of the gas phase at room temperature. The frequencies of the vibrations of the terminal BH_2 group in the spectrum of $Al(BH_4)_3$ are close to those of the corresponding vibratio in the infrared spectrum of diborane[61]. There is an

intense absorption band at 602 cm^{-1} belonging to the stretching vibrations of the Al—B bond. The intense absorption band corresponding to the B—B vibration is at 794 cm^{-1} in the diborane spectrum[61]. To understand the nature of the chemical bond in the $Al(BH_4)_3$ molecule, just as in other covalent tetrahydroborates, the ideas developed earlier by Lipscomb and coworkers[62] for boron hydrides can be applied. The molecular structure of aluminium tetrahydroborate can be interpreted as follows. Two types of bond ($BH_{termina}$ and Al—B) are "normal" two-centre bonds, for the formation of which the boron and aluminium atoms use three sp^2 hybrid atomic orbitals.

Table 2. Activity of the normal vibrations in the infrared and Raman spectra for prismatic and octahedral models.

Activity	No. of normal vibrations	Symmetry type	No. of normal vibrations	Activity
Raman	5	$A_1' > A_1$	7	Raman
—	2	A_1''		
—	3	$A_2' > A_2$	7	IR
IR	4	A_2''		
Raman, IR	9	$E' > E$	14	Raman, IR
Raman	5	E''		

The fourth atomic orbital of the boron, supposedly p_z, perpendicular to the plane in which lie the B—H and B—Al σ bonds, interacts with two s atomic orbitals of hydrogen atoms and one of the three pd^2 hybrid atomic orbitals of the aluminium atom to form four-centre molecular orbitals occupied by two electrons.

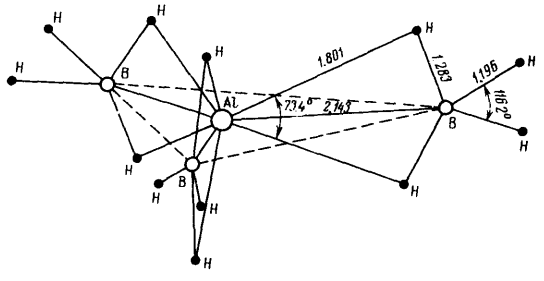


Figure 1. Model of the aluminium tetrahydroborate molecule.

Actually, the Al—B distance in the molecule is close to the sum of the so-called covalent radii and the BH_{bridge} and $Al—H_{bridge}$ distances are close to the corresponding distances in the B and Al hydrodes, in which these bonds are multicentre.

The crystal structure of aluminium tetrahydroborate was studied[60] in 1970. It forms two crystalline modifications (see Table 3) with enantiotropic transformation temperature of −76°C.

In the $Al(BH_4)_3$ crystal lattice all the intermolecular contacts are H---H contacts. The absence of any significant interaction between the molecules in the condensed phase explains the low melting point (−64.5°C) and boiling point (+44.5°C) of aluminium tetrahydroborate.

Table 3. Crystal-chemical results for the covalent tetrahydroborates.

Compound	Symmetry and unit-cell parameters				
	a, Å	b, Å	c, Å	space group	Z
α-Al $(BH_4)_3$	7.52	—	9.05	—	—
β-Al $(BH_4)_3$	7.50	12.15	5.94	$p2_12_12_1$	—
Be $(BH_4)_2$	13.59	—	9.92	$Aacd$	16
Zr $(BH_4)_4$	5.86	—	—	$p\bar{4}3m$	1

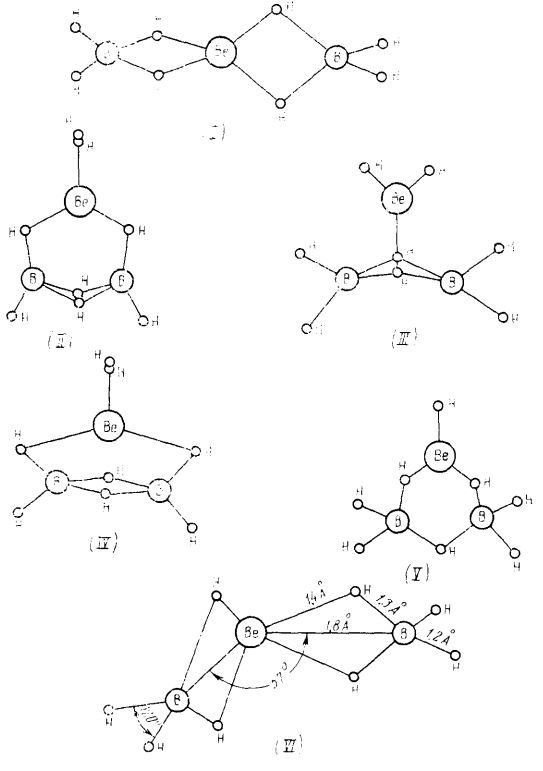


Figure 2. Molecular models of beryllium tetrahydroborate.

Silbiger and Bauer[54,63] were the first to investigate the molecular structure of beryllium tetrahydroborate $Be(BH_4)_3$ in the gas phase and they advanced two different interpretations of their experimental results. Both were based on the hypothesis of a linear configuration for the B—Be—B grouping. Fig. 2 (I) shows a model of the $Be(BH_4)_2$ molecule after Bauer[54]. Evidently, this model agrees well with classical views about the coordination four-covalency of beryllium.

In 1968 Almenningen and coworkers[1,64], in repeating the electron diffraction investigation of gaseous $Be(BH_4)_2$ by an improved experimental technique, came to an unexpected conclusion concerning the non-correspondence of Bauer's linear model with the experimental results. According to Almenningen, the three atoms (Be and B) are situated at the vertices of an almost regular triangle. The "triangular" configuration of the molecule agrees well with dipole moment (2.1 ± 0.5 D), measured[65] in 1969. Three polar molecular structures (Fig. 2, II, III, and IV) which exhibit the same symmetry C_{2v} can, in principle, be constructed on the base of the triangle of boron and beryllium atoms. Structures (II), (III), and (IV) are those of Almenningen, structure (V) was proposed by Cook[2] on the basis of a new interpretation (different from that of Almenningen and coworkers[1]) of the electron diffraction results.

Cook and Morgan[2] think that model (V) agrees better with the results of the investigation of the spectrum of beryllium tetrahydroborate, since it contains the $\diagdown BH_2$ grouping, which corresponds to the characteristic vibrations at 2630, 2531, and 974 cm^{-1} in the infrared spectrum†.

The presence of a band at 974 cm^{-1} is of special significance, since it has never before been observed in the infrared spectra of compounds with one terminal B—H bond[66].

In a further study of the infrared spectra of unsaturated vapour of $Be(BH_4)_2$ and its isotope-substituted analogues with ^{10}B and D, Cook and Morgan[67] were able to resolve P, Q, and R—the branches of the rotational structure in the spectrum. They showed the existence of terminal BH_2 groups and the absence of terminal BH groups in the $Be(BH_4)_2$ molecule.

An analysis of the vibrational-rotational contour of the absorption band with ν = 2521 cm^{-1} allowed the investigators to suggest the model of the $Be(BH_4)_2$ molecule shown in Fig. 2 (VI).

This model has C_{2v} symmetry. In the $\sigma_v(x, z)$ planes there are the boron atoms, the beryllium atom, and four terminal hydrogen atoms. The beryllium atom is linked with the boron atoms by twin hydrogen bridges. The planes of the bridging bonds are perpendicular to the $\sigma_v(x, z)$ plane.

The form of the infrared spectrum of saturated $Be(BH_4)_2$ vapour allowed the presence of polymeric beryllium tetrahydroborate molecules in this state to be proposed[67]. In 1952 Stosik[68] was the first to investigate the crystal structure of $Be(BH_4)_2$ (see Table 3), in 1952.

Marynick and Lipscomb[69] subsequently determined the dimensions and symmetry of the tetragonal unit cell more accurately (a = 13.62 ± 0.01 Å, c = 9.10 ± 0.01 Å, space group $I4\,Cd$) and interpreted the structure of beryllium tetrahydroborate in the crystalline phase.

In this structure the existence of polymeric spiral chains, not bonded to one another was observed. Polymerisation occurs owing to some of the BH_4 groups bonding beryllium atoms between them. The other BH_4 groups do not participate in the polymerisation and contain terminal BH_2 hydrogen bonds.

The structure of the zirconium tetrahydroborate $Zr(BH_4)_4$ molecule was investigated in both the crystalline and the gas phases by X-ray structural analysis and electron diffraction[70-72].

† The corresponding vibrations in the infrared spectrum of B_2H_6 are at 2612, 2525, 1035, and 979 cm^{-1}.

In every instance essentially the same result was obtained. The model of the $Zr(BH_4)_4$ molecule according to Plato and Heldberg's results[72] is shown in Fig. 3. Interestingly, in the $Zr(BH_4)_4$ molecule, unlike the $Al(BH_4)_3$ and $Be(BH_4)_2$ molecules, the $[BH_4]$ groups have C_{3v} symmetry and are connected with the zirconium atom by three hydrogen bridges. This symmetry of the BH_4 group and consequently of the molecular model with the metal atoms twelve-coordinated by hydrogen does not contradict the form of the infrared spectra of the zirconium and hafnium tetrahydroborates in the gas phase[73] and in solutions in non-polar solvents[73,74]. The intense absorption bands at 510 cm^{-1} and 602 cm^{-1} are assigned to the vibrations of the M—B bonds in zirconium and aluminium tetrahydroborates respectively. However, it is noteworthy that the spectrochemical investigations of these compounds are qualitative.

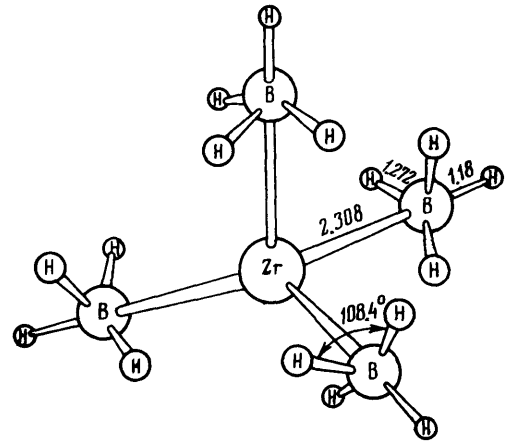


Figure 3. Model of the zirconium tetrahydroborate molecule.

The NMR spectrum of $Zr(BH_4)_4$ vapour[75] shows the equivalancy of all four protons in the BH_4 group. An analysis of the infrared spectrum of biscyclopentadienylzirconium bistetrahydroborate[76], that is, zirconium tetrahydroborate in which two BH_4 groups have been replaced by C_5H_5 groups, and an analysis of the infrared spectrum of $(C_5H_5)_2TiBH_4$ [77] showed the absence of absorption bands characteristic of BH_4^- ions in these compounds. The investigators suggested twin hydrogen bridging bonds between the boron atoms and the titanium and zirconium atoms. Consequently, unlike $Zr(BH_4)_4$, the local symmetry of the BH_4 group is C_{2v}. A comparison of the infrared spectra of these three compounds confirms the similarity of the infrared spectra of $(C_5H_5)_2Zr(BH_4)_2$ [76] and $TiBH_4(C_5H_5)_2$ and simultaneously the absence of the latter from the $Zr(BH_4)_4$ infrared spectra[73,74] in the range of the vibrations of the bridge and terminal B—H bonds, which shows that there are structural changes in the MBH_4 fragment in $(C_5H_5)_2Zr(BH_4)_2$ and $TiBH_4(C_5H_5)_2$ in comparison with $Zr(BH_4)_4$. The infrared spectra of the compounds $(Ph_3P_2)CuBH_4$,[78] $NiABH_4ClO_4$, and $NiA(BH_4)_2$ [79] (where A is 5,7,7,12,14,14-hexamethyl-1,4,8,11-tetra-azacyclotetradecane) were interpreted on the basis of models with M—H—B and terminal BH_2 bonds.

In view of the fact that the structure of the $Be(BH_4)_2$ molecule in the vapour is still the subject of discussion some spectroscopic investigations have been made[80,81], which seemed desirable for an attempt at interpreting the infrared spectra of the unsaturated vapour of $Be(BH_4)_2$ itself.

A spectroscopic study of $MeBeBH_4$ vapour showed[81] that its gas phase is a mixture of monomeric and dimeric molecules. An analysis of the lines of the infrared spectrum allowed Cook and Morgan[81] to conclude that for both the monomeric and the dimeric molecules the skeleton was linear. The absorption bands in the $MeBeBH_4$ spectrum were assigned on the basis of the infrared spectrum of the Me_2Be vapour[80] and of the results obtained in the replacement of the boron and hydrogen atoms in the $MeBeBH_4$ molecule by the isotopes ^{11}B and D.

These results seemed useful in the assignment of the absorption bands in the spectrum of the $Be(BH_4)_2$ molecule in the vapour[67]. According to this assignment the absorption band with wavenumber 1014 cm^{-1} corresponds to the vibration of the Be—B bond and the absorption bands with wavenumbers 2172, 2069, and 1545 cm^{-1} to the vibrations of the BeH_2B fragment of the $Be(BH_4)_2$ molecule.

Since the experimental results on which the structural chemistry of the covalent tetrahydroborates is based are few and not systematic, it is at present impossible to draw a reliable picture of the nature of the chemical bond in the $M(BH_4)_n$ molecules.

However, undoubtedly the classical ideas of the valence and stereochemical possibilities of the atoms of the light metals Be and Al seem inapplicable for describing the structure and chemical properties of these compounds.

V. CHEMICAL REACTIONS

1. REACTION OF THE TETRAHYDROBORATES $M(BH_4)_n$ WITH ALKENES

Reactions of this type have been studied only for aluminium tetrahydroborate. Gaseous aluminium tetrahydroborate reacts readily at room temperature with ethylene, propene, and but-1-ene[82]. As a result of the reaction boron alkyls are formed, presumably with alkyl-substituted aluminium tetrahydroborates. Since the reaction rate is independent of the alkene concentration, the following possible mechanism is proposed for it:

$$Al(BH_4)_3 \rightleftarrows Al(BH_4)_2H + BH_3\,, \quad (18)$$

$$Al(BH_4)_2H + CH_2=CHR \rightarrow Al(BH_4)_2CH_2CH_2R\,, \quad (19)$$

$$BH_3 + 3\,CH_2=CHR \rightarrow B(CH_2CH_2R)_3\,. \quad (20)$$

The conversion rate is increased in the presence of traces of oxygen. The final products (boron alkyls) are inhibitors[82,83]. The reaction of aluminium tetrahydroborate with butadiene is more complex and evidently is not described by such a simple scheme[83].

2. REACTION WITH COMPOUNDS CONTAINING AN M—R BOND

Uranium tetrahydroborate reacts with trimethylboron at 50—60°C with the formation of methyldiborane and a green viscous liquid. Its fractionation allows us to obtain compounds of composition $U(BH_4)_3(CH_3BH_3)$ and $U(BH_3CH_3)_4$, which react with water, hydrogen chloride, and diborane, with the formation of methylboric acid or methyldichloroborane, uranium tetrahydroborate, and alkyl-substituted boranes[22]:

$$U(BH_3CH_3)_4 + 12\,HCl \rightarrow UCl_4 + 12H_2 + 4CH_3BCl_2\,, \quad (21)$$

$$U(BH_3CH_3)(BH_4)_3 + 12\,H_2O \rightarrow U(OH)_4 + 15\,H_2 + CH_3B(OH)_2 + 3HBO_2\,, \quad (22)$$

$$U(BH_3CH_3)(BH_4)_3 + B_2H_6 \rightarrow U(BH_4)_4 + CH_3BH_2BH_3\,, \quad (23)$$

$$U(BH_3CH_3)_4 + B_2H_6 \rightarrow U(BH_4)_4 + (CH_3)_4B_2H_2\,. \quad (24)$$

Reactions analogous to those described above, namely those leading to complication of the BH_4 group without change in the AlH_nB-bridging bonds are also known for aluminium tetrahydroborate, since its reaction with tetraborane and decaborane in ether lead to the formation of a series of compounds $Al(BH_4)_{3-x}(B_3H_8)_x$, where $x = 1$, 2, or 3, and $Al(BH_4)_{3-x}(B_{10}H_{13})_x$, where $x = 1$ and 2, respectively[84].

Aluminium tetrahydroborate[85] reacts vigorously with tetramethyltin and tetramethyl-lead with the formation of intermediate unidentified solid products, which decompose into Sn or Pb, H_2, methylated boranes, and $CH_3Al(BH_4)_2$. It is assumed that the intermediate unstable products have the composition $(CH_3)_2Sn(BH_4)_2$ and $(CH_3)_3Pb(BH_4)$. Aluminium tetrahydroborate reacts with trimethylchlorosilane according to the equation:

$$2\,Al(BH_4)_3 + 6\,(CH_3)_3SiCl \rightarrow 2AlCl_3 + 3B_2H_6 + 6\,(CH_3)_3SiH\,. \quad (25)$$

However, in silicon tetrachloride hydrogenation of the Si—Cl bonds by aluminium tetrahydroborate does not take place[86].

3. REACTION WITH OTHER ORGANIC COMPOUNDS

With organic and organosilicon compounds which are capable of being reduced the covalent tetrahydroborates react as very strong reductants. An example is the reaction of uranium tetrahydroborate with methyl borate[22]:

$$6\,U(BH_4)_4 + 2\,B(OCH_3)_3 \rightarrow 6\,U(BH_4)_3(BH_3OCH_3) + B_2H_6\,, \quad (26)$$

or that of aluminium tetrahydroborate with ethyl orthosilicate[85]:

$$2\,Al(BH_4)_3 + Si(OC_2H_5)_4 \rightarrow 2\,B_2H_6 + SiH_4 + 2Al(BH_4)\cdot(OC_2H_5)_2\,. \quad (27)$$

4. REACTION WITH NUCLEOPHILIC AGENTS—WITH NEUTRAL MOLECULES (L) OR IONS (X^-)

Reactions of this type are of the greatest interest. They are specific for the covalent tetrahydroborates and allow compounds of a new type to be obtained, containing Al and Be atoms in unusual valence states.

a. Formation of Compounds Containing the Anionic Complexes $[M(BH_4)_nX]^-$

The first mention of the formation of the complexes $M'X.M''H_n.mBH_3$, where M' is an alkali metal and M'' = Al or Be, was made in Wiberg's patents[87,88] in which the possibility of obtaining such compounds by the action of the corresponding covalent tetrahydroborate or of its ethereal solutions on the salts of alkali metals, or by the reaction of lithium tetrahydroaluminate with diborane in ethereal solutions was mentioned. In the latter instances, complexes containing the ether were formed.

Nöth[9], in referring to unpublished results[89], suggested the formation of such compounds in the reaction mixture in the production of aluminium tetrahydroborate by reaction (2).

Ashby and Foster[90] subsequently queried the existence of complexes in ethereal solutions. Later investigations of Nöth and coworkers[91] showed the possibility of the existence of equilibria in the $MX-Al(BH_4)_3-Et_2O$ systems:

$$Al(BH_4)_3 + LiX \xrightarrow{Et_2O} Li[Al(BH_4)_3X] \rightleftarrows LiBH_4 + Al(BH_4)_2X . \quad (28)$$

Complexes stable at room temperature were also obtained containing large organic or inorganic cations $[N(C_2H_5)_4][Al(BH_4)]_4$,[92] $[(C_8H_{17})_3NC_3H_7][Al(BH_4)_4]$, $[(C_8H_{17})_3NC_3H_7][Be(BH_4)_3]$, $[(C_8H_{17})_3NC_3H_7]_2[Be(BH_4)_5]$,[93] $[(C_4H_9)_4N][Al(BH_4)_4]$,[94] $K[Al(BH_4)_3Cl]$, and $K[Al(BH_4)_4]$.[95]

The stability of complexes with complex anions is known to depend on the charge: radius ratio of the outer-sphere cation z/r. For example, in the series $LiAlH_4-KAlH_4$ or $LiBH_4-KBH_4$ the thermal stability of the compounds increases rapidly. There is a similar regularity in the present instance. Actually, when the vapour pressure of aluminium tetrahydroborate above the complex $Li[Al(BH_4)_4]$ [88] is 2 mmHg the complexes with large organic cations, for example, $[N(C_2H_5)_4][Al(BH_4)_4]$ do not dissociate into the initial products even at 140°C.[92,94] The compounds $K[Al(BH_4)_3Cl]$ and $K[Al(BH_4)_4]$ probably have a somewhat lower stability and disproportionate at 130°C with an appreciable endothermic effect. It is noteworthy that the decomposition of the complexes at this temperature differ; whereas the complex $K[Al(BH_4)_4]$ dissociates mainly into the initial KBH_4 and $Al(BH_4)_3$, the compound $K[Al(BH_4)_3Cl]$ decomposes according to the following probable mechanism:

$$K[Al(BH_4)_3Cl] \rightarrow Al(BH_4)_2Cl + KBH_4 , \quad (29)$$

$$Al(BH_4)_2Cl \rightarrow Al(BH_4)_3 + AlCl_3$$

$$Al(BH_4)_2Cl \rightarrow AlB_xH_yCl + B_2H_6 + H_2 . \quad (30)$$

The NMR spectrum of solutions of the complexes $[(C_8H_{17})_3NC_3H_7][M(BH_4)_n]$ suggests the equivalence of all the BH_4 groups in the $[M(BH_4)_n]^{m-}$ anion[93].

b. Reaction with the Formation of Molecular Compounds of the $M(BH_4)_n.mL$ Type

Oxonium and sulphonium complexes. Beryllium and aluminium tetrahydroborates dissolve in ethers with considerable evolution of heat and with the formation of complexes, the composition and properties of which are given in Table 4.

The reactivity of the oxonium complexes and of their solutions is less than that of the initial tetrahydroborates—in air, they are oxidised and hydrolysed slowly, without spontaneous combustion; it reacts violently with water, but without explosion. At room temperature in a dry atmosphere the oxonium complexes are relatively stable and decompose at an appreciable rate only at 40—50°C.

Desolvation of the oxonium complexes is accompanied by decomposition of the molecules of the tetrahydroborate and ligand[34].

It is known that the equilibrium in the system:

$$Al(BH_4)_3Me_2S + Me_2O \rightleftarrows Al(BH_4)_3Me_2O + Me_2S \quad (31)$$

is shifted almost entirely to the side of the formation of $Al(BH_4)_3Me_2O$, which shows that the strength of the oxonium Al←O bond is greater than that of the sulphonium Al←S bond.

In several instances the interaction of tetrahydroborates with liquid and solid ligands is identical. For example, beryllium tetrahydroborate reacts with THF vapour at room temperature to form the saltlike complex $Be(C_4H_8O)_4(BH_4)_2$,[27] in the infrared spectrum of which absorption bands characteristic for the isolated BH_4^- group are present. In the reaction of the same compounds in the liquid phase a vitreous substance of indefinite composition is formed[27]. This is probably brought about by irreversible interaction of the complex formed initially with the excess of ligand. The corresponding complex of aluminium tetrahydroborate reacts with the excess of THF with loss of a BH_3 group[34], evidently in the form $BH_3.C_4H_8O$.

Table 4. Some physicochemical properties of oxonium complexes of beryllium, aluminium, and zirconium tetrahydroborates.

Compound	M.p., °C	p_{sat}, mmHg
$Be(BH_4)_2 \cdot Et_2O$	liquid at 20°C	—
$Be(BH_4)_2 \cdot 4C_4H_8O$	solid at 20°C	—
$Al(BH_4)_3 \cdot Me_2O$	0—1	0.5 at 20°C
$Al(BH_4)_3 \cdot Et_2O$	0.5—1.5	7.8 at 85°C
$Al(BH_4)_3 \cdot C_4H_8O$	24—26	—
$2[Be(BH_4)_2] \cdot 3[C_2H_4(OMe)_2]$	solid at 20°C	—
$Zr(BH_4)_4 \cdot C_4H_8O$	2	—

Oxonium complexes can also be obtained by other methods, for example, by reaction (12), which allows compounds of different composition described by the formula $H_nAl(BH_4)_{3-n}.xEt_2O$, where $x = 1$ or 2, to be obtained from the same initial substances taken in equal ratios. The second molecule of the ether in such complexes is weakly bound with the $H_nAl(BH_4)_{3-n}$ molecule and is readily removed in a vacuum. At elevated temperatures the decomposition of the complex proceeds further[34]. The diethyl ether in the compounds $H_nAl(BH_4)_{3-n}.xEt_2O$ is readily replaced by an equimolecular amount of THF:

$$H_nAl(BH_4)_{3-n} \cdot xEt_2O + xC_4H_8O \rightarrow H_nAl(BH_4)_{3-n} \cdot xC_4H_8O + xEt_2O \quad (32)$$

The thermal decomposition of the compound $HAl(BH_4)_2.2C_4H_8O$ was studied and takes place with the formation of butoxyaluminium bistetrahydroborate:

$$2HAl(BH_4)_2 \cdot 2C_4H_8O \rightarrow 2C_4H_8O + (BH_4)_2Al\langle O(C_4H_9)\rangle Al(BH_4)_2 . \quad (33)$$

In addition to complexes with ethers, aluminium tetrahydroborate forms stable compounds of the $Al(BH_4)_3 \cdot Al(OR)_3$ type on reacting with the corresponding alkoxides. The complexes obtained are liquids or solids, which vaporise without decomposition in a high vacuum[96].

Systems which contain ethers and heavy metal tetrahydroborates have been studied insufficiently. It is only known that when Zr tetrahydroborate reacts with THF the compound $Zr(BH_4)_4.C_4H_8O$ is formed[96].

The existence of this compound was found on the basis of a study of the equilibrium diagram in the $Zr(BH_4)_4-C_4H_8O$ system. Interestingly, on the equilibrium diagrams

of the $Zr(BH_4)_4$—dioxan[98], $Zr(BH_4)_4$—n-C_6H_{14}, $Zr(BH_4)_4$—cyclo-C_6H_{12}, $Zr(BH_4)_4$—C_6H_6, and $Zr(BH_4)_4$—$C_6H_6Zr(BH_4)_4$—$C_6H_5CH_3$ [99] systems there are only simple eutectics. It is noteworthy that neither structural nor physicochemical investigations of the oxonium complexes of the tetrahydroborates of aluminium, beryllium, and the Group metals have yet been made.

Compounds with Ammonia. The reaction of covalent tetrahydroborates with ammonia has been studied only for aluminium tetrahydroborate. In various investigations[3,5,28,100,101] the existence of several compounds has been found: $Al(BH_4)_3.nNH_3$, where n = 1, 2, 4, and 6. The aluminium tetrahydroborate ammines are solid substances stable at room temperature. The first to be obtained was aluminium tetrahydroborate monoammine, by the reaction of $Al(BH_4)_3$ with ammonia, taken in equimolecular proportions, initially at −80°C and then at room temperature. An attempt by Bird and Wallbridge[5] to prepare the monoammine in toluene solution at 1 : 1 molar ratio of the reagents and −78°C led to the production of aluminium tetrahydroborate diammine. A solution of the hexa-ammine complex is formed in the reaction of aluminium tetrahydroborate with an excess of liquid ammonia.

Another method for making an ammoniacal solution of the hexammine complex is the electrolysis of alkaline tetrahydroborates in liquid ammonia:

$$3\,NaBH_4 + Al + 6NH_3 \rightarrow Al(BH_4)_3 \cdot 6\,NH_3 + 3\,Na\,. \qquad (34)$$

A dissolving anode served as a source of aluminium[102]. When ammonia was removed from the solution, aluminium tetrahydroborate hexammine, stable at room temperature, was precipitated; it evidently contained clathrate ammonia[3]. X-Ray diffraction analysis showed the crystal structure of only a clathrate of composition $Al(BH_4)_3.6.7NH_3$.[3,5,99,101]. The infrared and NMR spectra show the presence of BH_4^- ions in the hexammine[5]. The ammoniacal solutions of aluminium tetrahydroborate hexammine evidently contain these ions, which react with aluminium chloride to form aluminium chloride hexammine and hydrogen:

$$Al(BH_4)_3(NH_3)_6 + 6\,NH_4Cl \rightarrow AlCl_3(NH_3)_6 + 3\left[\begin{matrix}NH_3\\NH_3\end{matrix}\!\!>\!BH_2\right]Cl + 6H_2\,. \qquad (35)$$

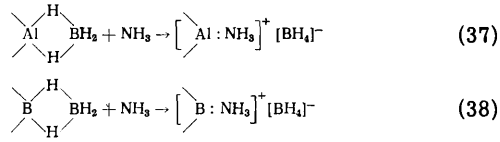
The reaction of aluminium tetrahydroborate hexammine with lithium in ammonia at −40°C proceeds according to the equation:

$$Al(NH_3)_6(BH_4)_3 + 2Li \rightarrow Li[Al(NH_2)_2(BH_4)_2] + H_2 + LiBH_4 + 4NH_3\,. \qquad (36)$$

The composition of the compound $Li[Al(NH_2)_2(BH_4)_2]$ was found by chemical analysis. Bird and Wallbridge[5] postulated the possibility of the $Al(H_2N)_2^+$ grouping in the anion of this complex being isoelectronic with allene $CH_2{=}C{=}CH_2$ and examined the possibility of its stabilisation according to the scheme $[H_2N{=}Al{=}NH_2]^+$.

Unlike aluminium tetrahydroborate its hexammine is slowly hydrolysed by cold water and is stable when heated to 50°C. When it is kept for a long period (11 days) at 50°C in a vacuum (10^{-5} mmHg) it yields a solid residue stable up to 400°C and the release of ammonia and volatile boron-containing compounds. Heating for 8 h at 105°C leads to the formation of analogous products[100].

Evidently, saltlike aluminium tetrahydroborate hexammine is the final product of the reaction between $Al(BH_4)_3$ and ammonia. Heterolytic breaking of the AlH_2B bridging bonds, which occurs in the $Al(BH_4)_3$ molecule under the action of NH_3, is analogous to the formation of the so-called "diborane ammine":



$$Al(H)_2BH_2 + NH_3 \rightarrow [Al:NH_3]^+[BH_4]^- \qquad (37)$$

$$B(H)_2BH_2 + NH_3 \rightarrow [B:NH_3]^+[BH_4]^- \qquad (38)$$

It seems that the initial stage of this process is the formation of unstable non-saltlike addition products of the $Al(BH_4)_3.nNH_3$ type; these may include the monoammine and diammine described earlier[4,28].

Compounds with primary and secondary amines, phosphines, and hydrazine. Nothing has been published on the reaction of aluminium tetrahydroborate with primary and secondary amines, phosphines, and hydrazine. Beryllium tetrahydroborate forms the following complexes with these ligands: $Be(BH_4)_2.NH(CH_3)_2$; $Be(BH_4)_2.3NH(CH_3)_3$; $Be(BH_4)_2.PH(CH_3)_2$; $Be(BH_4)_2.4NH_2.(C_4H_9)$;[102-103] $Be(BH_4)_2.3N_2H_4$.[104]

The monodimethylamine and phosphine derivatives are liquids; the others are crystalline[103-105]. It is suggested that like $Be(BH_4)_2.4C_4H_8O$ the complex of monobutylamine with beryllium tetrahydroborate has a saltlike structure with a BH_4^- anion[103].

The melting point has been measured only for tris(dimethylamine)beryllium tetrahydroborate (94°C), which decomposes at that temperature with release of hydrogen and the amine.

Compounds with tertiary amines, phosphines, and trimethylarsine. 1:1 complexes of beryllium and aluminium tetrahydroborates with tertiary amines or phosphines are obtained at low temperatures in the absence of an excess of the ligand. It is convenient to carry out the reaction in the presence of an inert solvent[104,106].

Table 5. Physicochemical properties of complexes of composition $M(NH_4)_nL$.

Compound	M.p., °C	T_{decomp}, °C	Other properties
$Be(BH_4)_2 \cdot N(CH_3)_3$	35	~140	$\lg P_{mmHg} = 8.353 - 2909/T$
$Al(BH_4)_3 \cdot N(CH_3)_3$	79 in rapid heating	50	monomer in vapour monomer in C_6H_6
$Al(BH_4)_3 \cdot N(C_2H_5)_3$	solid at 25°C	50	monomer in C_6H_6
$Be(BH_4)_2 \cdot P(CH_3)_3$	liquid at 20°C	--	volatile in a vacuum
$Be(BH_4)_2 \cdot P(C_2H_5)_3$	liquid at 20°C	—	P_{mmHg} = 0.01 at 68°C
$Be(BH_4)_2 \cdot PPh_3$	163 (decomp.)	122	monomer in C_6H_6
$Al(BH_4)_3 \cdot P(CH_3)_3$	78	—	monomer in C_6H_6
$Al(BH_4)_3 \cdot PPh_3$	186 (decomp.)	>70	monomer in C_6H_6
$Al(BH_4)_3 \cdot As(CH_3)_3$	57	—	—

Compounds of composition $M(BH_4)_n.L$ have been studied in relative detail. The physicochemical properties of such complexes are in Table 5.

As Table 5 shows, the 1 : 1 compounds are stable under ordinary conditions. The decomposition temperatures of most of the compounds have been determined but their pyrolysis has been insufficiently studied. An analysis of

published papers suggests that during the pyrolysis trialkylaminoboranes or trialkylphosphineboranes are formed, which are evidently thermodynamically the most stable compounds in the "ternary systems" MH_n—B_2H_6—NR_3 or MH_n—B_2H_6—PR_3.[4,28]

The amine and phosphine complexes of aluminium tetrahydroborate react with an excess of the ligand according to the following probable equation:

$$Al(BH_4)_3L \overset{+L}{\rightleftarrows} Al(BH_4)_3 \cdot 2L \rightleftarrows 'Al(BH_4)_2HL + BH_3L \overset{+L}{\rightleftarrows} \ldots\ldots \overset{+L}{\rightleftarrows} AlH_3 \cdot L \ddagger \quad (39)$$

Unlike the complexes of aluminium tetrahydroborate with tertiary amines and phosphines, the arsonium complex of composition $Al(BH_4)_3.As(CH_3)_3$ does not react with an excess of the ligand. The complex readily participates in an exchange reaction with trimethyl phosphine with the formation of $Al(BH_4)_3.P(CH_3)_3$, which is probably due to the greater strength of the Al←P bond compared with that of Al←As.

As already noted, beryllium tetrahydroborate does not form 1 : 2 complexes with trimethylamine and trimethylphosphine. When the trimethylamine complex of beryllium tetrahydroborate is heated it reacts with an excess of trimethylamine thus[29]:

$$Be(BH_4)_2 \cdot N(CH_3)_3 + N(CH_3)_3 \xrightarrow{100^\circ} \{HBe(BH_4)N(CH_3)_3\}_n + BH_3N(CH_3)_3 \quad (42)$$

The reaction of the phosphine complex of beryllium tetrahydroborate with an excess of the ligand evidently leads to the formation of beryllium hydride, which contains a certain amount of trialkylphosphine[102,103]:

$$Be(BH_4)_2 \cdot PR_3 + PR_3 \xrightarrow{70-180^\circ} \{BeH_2\}_n + 2PR_3BH_3 \quad (43)$$

The infrared spectra of compounds of aluminium tetrahydroborate and tetradeuterioborate with $N(CH_3)_3$, $P(CH_3)_3$, $As(CH_3)_3$, Et_2O, Me_2O, and Me_2S have been recorded[5,110] in the range 400—4000 cm^{-1}. Quantitative analysis and comparison of these spectra allows the following conclusions to be drawn:

1. Usually the frequencies of the vibrations in the coordinated $Al(BH_4)_3$ molecule are hardly displaced at all in comparison with the frequencies of the vibrations in free compounds.
2. Judging by the positions of the absorption bands characteristic for terminal BH_2 bonds, the structure of the tetrahydroborate group in the $Al(BH_4)_3.L$ molecules remains approximately the same as in the initial aluminium tetrahydroborate.
3. The equivalency of the three BH_4 groups in the $Al(BH_4)_3.L$ molecules can be postulated, since the significant splitting of the absorption bands belonging to the Al—H and B—H bridging vibrations was not observed.
4. The absorption bands due to the Al—B vibrations are shifted in the infrared spectra of the complexes into the longwave range, which can be interpreted as an increase in the Al—B interatomic distance, due to an expansion of the coordination sphere of the Al atom and an increase in its coordination number.

‡ The compounds $AlH_x(BH_4)_{3-x}L$, which are intermediates in reaction (39), were obtained independently by the reaction:

$$AlCl_{3-x}H_xN(CH_3)_3 + LiBH_4 \xrightarrow{C_6H_6} AlH_x(BH_4)_{3-x} \cdot N(CH_3)_3 + LiCl \quad (40)$$

Trialkylsiloxane derivatives of aluminium tetrahydroborate can be obtained in a similar manner:

$$R_3SiOAlCl_2 + 2LiBH_4 \xrightarrow{Et_2O} R_3SiOAl(BH_4)_2 + LiCl \quad (41)$$
$$(R = CH_3 \text{ or } C_2H_5)^{109}$$

However, these conclusions do not agree completely with the results of a direct X-ray diffraction investigation of the molecular structure of the complex $Al(BH_4)_3.N(CH_3)_3$.[111,112] Bird and Wallbridge observed two different molecular configurations of the complex $Al(BH_4)_3.N(CH_3)_3$. —"high-temperature" and "low temperature".

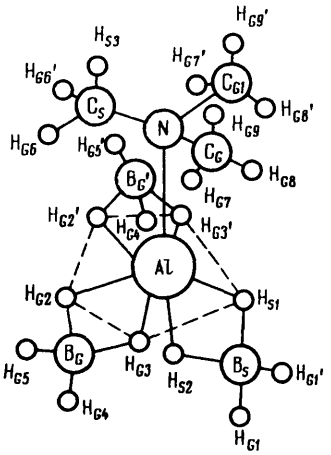


Figure 4. Model of a molecule of the compound $Al(BH_4)_3.N(CH_3)_3$.

In the "high-temperature" modification the B and N atoms are situated at the vertices of an almost regular tetrahedron, at the centre of which is the Al atom. The coordinates of the H atoms were not determined in this study, therefore the form and symmetry of the $[AlX_n]$ polyhedron, where X = N, B, or H cannot be determined.

Evidently, the investigations[5,11] of the infrared spectra relate to this configuration of the $Al(BH_4)_3.N(CH_3)_3$ molecule. An investigation of the low-temperature configuration at −160°C was more complete. The model of the $Al(BH_4)_3.N(CH_3)_3$ molecule is given in Fig. 4; Table 6 gives the valence angles and interatomic distances.

The boron atoms in the $Al(BH_4)_3.N(CH_3)_3$ molecule are clearly non-equivalent, the Al—H_{bridge} distances differing markedly from one another: from 1.75—1.83 Å for the Al—B_G group to 1.95—2.00 Å for the AlB_S group.

The coordination polyhedron around the aluminium atom is a distorted pentagonal bipyramid. Interestingly, whereas the Al—N interatomic distance is almost equal to the sum of the covalent radii of Al and N and does not differ from the Al—N interatomic distances in the molecules of the trialkylaminealanes $AlH_3.nNR_3$,[114] the Al—B interatomic distance is considerably greater than that in the $Al(BH_4)_3$ molecule, 2.257 Å compared with 2.14 Å.

An analysis of the structure suggests that it is produced by the displacement of one of the BH_4 groups, namely the group situated in the "trans position" to the $N(CH_3)_3$ molecule.

Actually, under the action of an excess of the ligand such a displacement takes place very readily, as already noted above . Evidently, in the $Al(BH_4)_3.N(CH_3)_3$ molecule and in the molecules (monotypical with it) of the complexes with trimethylphosphine, trimethylarsine,

triethylamine, etc., the atom for the formation of four two-centre bonds (three Al—B and one Al—L) uses a set of four sp^3 hybrid atomic orbitals.

Table 6. Valence angles and interatomic distances for the low-temperature configuration of $Al(BH_4)_3.N(CH_3)_3$.

$r_{Al-N} = 1.989 \pm 0.008$ Å	$B_S H_4$: $r_{B_S-H_{S1}} = 1.48 \pm 0.10$Å
$r_{Al-B_S} = 2.257 \pm 0.012$ Å	$r_{B_S-H_{S2}} = 1.16 \pm 0.011$Å
$r_{Al-B_G} = 2.227 \pm 0.011$Å	$r_{B_S-H_{G1}} = 1.15 \pm 0.08$Å
$r_{Al-H_{S1}} = 2.00 \pm 0.10$Å	$r_{H_{S1}-H_{S2}} = 2.29 \pm 0.15$Å
$r_{Al-H_{S2}} = 1.95 \pm 0.11$Å	$B_G H_4$: $r_{B_G-H_{G2}} = 1.18 \pm 0.07$Å
$r_{Al-H_{G2}} = 1.83 \pm 0.07$Å	$r_{B_G-H_{G3}} = 1.40 \pm 0.07$Å
$r_{Al-H_{G3}} = 1.75 \pm 0.08$Å	$r_{B_G-H_{G4}} = 1.22 \pm 0.11$Å
$\angle (N-AlH_{S2}) = 152.8 \pm 3.3°$	$r_{H_{G2}-H_{G3}} = 2.06 \pm 0.10$Å

The three four-centre AlH_2B bonds are formed from the *d* atomic orbital of the aluminium without participation of the *p* atomic orbital as in the $Al(BH_4)_3$ molecule. Because of this the strength of the bridging bonds in the $Al(BH_4)_3.L$ molecule should evidently be less than in the aluminium tetrahydroborate molecule. It is noteworthy that the existence of complexes of composition $Al(BH_4)_3.2L$ (see p. 10) does not contradict the above views.

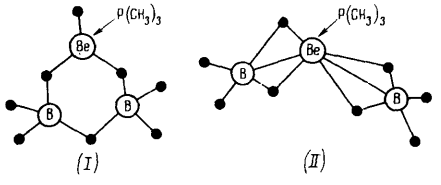


Figure 5. Probable structures of the $Be(BH_4)_2.P(CH_3)_3$ molecule.

The molecular structures of such compounds is of considerable interest. It can be postulated that the coordination polyhedron of the aluminium atom formed by the B and L atoms will be like that in the molecule of bistrimethylamine alane $AlH_3.2N(CH_3)_3$ with location of the boron atoms in the equatorial plane of the trigonal bipyramid.

X-Ray diffraction investigations of the complex derivatives of beryllium, zirconium, hafnium, thorium, and uranium tetrahydroborates have not yet been made.

A qualitative analysis of the infrared and NMR spectra of the compound $Be(BH_4)_2.P(CH_3)_3$ [103,104] allowed it to be ascribed the probable structure shown in Fig. 5 (I).

However, taking into account the most recent results on the structure of beryllium tetrahydroborate in the gas phase[68] another model of the structure of the $Be(BH_4)_2.PMe_3$, Fig. 5 (II), seems more probable.

It must be noted that the addition of a second molecule of the ligand to a beryllium tetrahydroborate molecule is always accompanied by the breaking of the Be—H—B bridging bonds. For example, the complexes $Be(BH_4)_2.4C_4H_8O$ and $Be(BH_4)_2.4C_4H_9NH_2$ are constructed from $[Be.4L]^{2+}$ cations and $[BH_4]^-$ anions[102].

This experimentally established fact can be explained as the consequence of the beryllium atom in the $Be(BH_4)_2L$ molecule using the entire set of four atomic orbitals and becoming "coordination saturated" as a result. It is to be hoped that further investigation of the structure and reactivity of the complexes of the tetrahydroborates of the light metals will yield results convenient for developing new ideas about the stereochemistry and nature of the chemical bond in the inorganic compounds of the light elements.

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Department of Inorganic
Chemistry, Moscow
State University

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Electrochemical Behaviour of Uranium at a Mercury Electrode in Aqueous Solutions

R.Sh.Enikeev, S.I.Khan, and M.T.Kozlovskii (deceased)

In aqueous solutions hexavalent uranium is reduced at a mercury electrode to the quadrivalent or tervalent state and in some cases even to the metal itself. The number of stages observed in the cathodic process and also the final valence form of uranium depend on the composition of the solution, in particular on the presence of complex-forming agents and the pH of the medium. As an analytical method, the polarography of uranium is at present finding only limited applications. The bibliography includes 131 references.

The first studies dealing with the electrolysis of aqueous solutions of uranium salts at a mercury cathode were published in 1880.[1-2] In these and in subsequent investigations[3-9] carried out in 1901—1919, it was shown that a uranium amalgam is not formed when aqueous solutions of uranium(VI) chlorides, sulphates, nitrates, acetates, and carbonates are electrolysed, since, depending on the initial pH, precipitates of tetravalent or hexavalent uranium are deposited at the mercury cathode owing to the increase of the alkalinity of the solution during electrolysis (in the absence of effective complex-forming agents from the solution, hexavalent uranium is precipitated at pH > 4.5 and tetravalent uranium at pH > 3.5).[10-13] Indeed, the reduction of hexavalent uranium at the cathode involved hydrogen ions in accordance with the mechanism[10,14]

$$UO_2^{2+} + 4H^+ + 2e \rightarrow U^{4+} + 2H_2O,$$

while in the anodic process fewer hydrogen ions are produced for the same consumption of electricity:

$$H_2O - 2e \rightarrow 2H^+ + \frac{1}{2}O_2.$$

On the other hand, in the presence of ions which are oxidised at the anode, for example chloride or acetate ions, the increase in the alkalinity of the solution is more pronounced. For this reason, it is now generally believed that in the electrolysis of its aqueous solutions uranium is not reduced to the metal at a mercury cathode[10-12,15-18]. (The potential of the U^{3+}/U_{met} system is -1.8 V relative to that of the hydrogen electrode[19].) Moreover, in analytical practice electrolysis at a mercury cathode is a known method for the elimination of metallic impurities from uranium[10,14,20-24].

In 1901 a report was published claiming the preparation of a uranium amalgam by the electrolysis of a hydrochloric acid solution of uranium(IV) at a mercury cathode[25]. The author quotes in support of his claim the finding that the residue after vacuum distillation of mercury is pyrophoric. However, according to the literature, pyrophoric properties are characteristic not only of metallic uranium but also of some of its oxides[7,26,27]. Later special investigations[28,29] failed to confirm this report[25].

According to another report[29], the electrolytic preparation of uranium amalgam from aqueous solutions is possible only when certain conditions are fulfilled, namely a high acidity of the electrolyte ($>2\,N\ H_2SO_4$), a high cathodic current density (more than 6 A cm^{-2}), and intense cooling of the solution. Under these conditions, about 1 ml of amalgam paste containing 0.5 g of metallic uranium (3.3 wt.%), the solid phase of which can be separated from the liquid on a glass sinter, is formed after 4 h.

According to communications by the same investigators[29,30], uranium(VI) can be reduced to the metal not only by electrolysis at a mercury cathode, but also by incorporation with zinc and tin amalgams; this contradicts a number of literature data, which indicate that zinc and its amalgam can reduce uranium(VI) only to the tervalent state and tin amalgam can reduce it only to the quadrivalent state[10,14,23,31-33].

In the electrolysis of solutions of hexavalent and tetravalent uranium at moderate current densities (less than 0.5 A cm^{-2}) at a mercury cathode, uranium may be reduced at most to the tervalent state[28].

It has been claimed[34] that uranium amalgam containing about 0.016 wt.% of the metal may be obtained by the incorporation of hexavalent uranium with sodium amalgam (0.13 wt.%) in acetate solutions at pH 4.

In the electrolysis of aqueous solutions of uranium(VI) at solid cathodes (Pt, Al, Ta, Nb, Cu, Pb, etc.), crystalline cathodic deposits are formed[2,9,35-45]: UO_2 or UF_4 (in the electrolysis of fluoride solutions), which is used for the preparation of samples of uranium in the determination of its isotopic composition by the α-spectrometric method. Partial or complete replacement of water by organic solvents improves somewhat the physical properties of these deposits (density, uniformity of distribution on the surface of the cathode) without, however altering their composition[2,9,10,46-49]. The report[48] that uranium may be reduced to the metal at a solid cathode in anhydrous alcoholic solution was not confirmed[27].

Thus in the electrolysis of aqueous and non-aqueous solutions, uranium is not reduced to the metal at solid cathodes. On the other hand, the possibility of reducing uranium to the metal at a mercury cathode is due to the fact that uranium forms intermetallic compounds with mercury[11] which shifts the potential of the U^{3+}/U_{met} system towards less negative values. The formation of uranium amalgam is also promoted by a high overvoltage for the discharge of hydrogen ion at the mercury electrode.

As shown above, the principal aim of the studies on the electrolysis of solutions of various uranium compounds was to find the limiting degree of its reduction and in particular to elucidate the possibility of an electrolytic preparation of uranium amalgam. On the other hand, the kinetics of the stepwise transition of uranium from the highest to the lowest valence states were not as a rule studied. In this connection, polarographic data are of definite interest for the investigation of the electrochemical behaviour of uranium at a mercury electrode.

The first studies on the polarography of hexavalent uranium were published in 1925 and 1928.[50-52] It was stated that in hydrochloric acid solutions at pH 1—2 multistage reduction of hexavalent uranium to the tervalent states takes place at a dropping mercury electrode (d.m.e.

Starting in 1945, the publication of a series of studies devoted to the systematic investigation of the polarographic behaviour of uranium began. One should note that most of these studies were carried out to extend the analytical applications of polarography[10,23] and relatively few[53-62] were concerned primarily with the electrochemical behaviour of uranium at a mercury electrode. In particular, it was shown that the reduction of hexavalent uranium at a dropping mercury electrode is a multistage process which depends significantly on the composition of the solution. In acid solutions of uranium(VI) free from complex-forming agents, for example in chloride or perchlorate solutions, two principal waves are observed[53-69] (Fig. 1). The first wave in the range of potentials between 0.12 and −0.28 V (s.c.e.)† is generally believed to correspond to the reversible reduction of sexivalent uranium to the pentavalent state. With increase of the acidity of the solution above 0.1 *N*, the half-wave potential for the first stage in the reduction of hexavalent uranium shifts towards negative values[53] and the height of the wave increases if the uranium(VI) concentration remains constant. This phenomenon is explained in the following way[53]. Pentavalent uranium, formed as a result of the electrode reaction disproportionates according to the following mechanisms depending on the acidity of the solution[53-69]:

$$2\,UO_2^+ + H^+ \rightarrow UO_2^{2+} + UOOH^+ \quad (\text{at pH} < 1),$$

$$2\,UO_2^+ + 2\,H^+ \rightarrow UO_2^{2+} + UO^{2+} + H_2O \quad (\text{at pH} > 1).$$

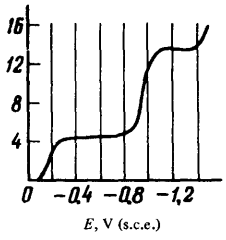


Figure 1. Polarogram for the reduction of uranium(VI) in 10^{-3} M UO_2Cl_2 + 0.03 M HCl + 0.1 M KCl solution containing 2×10^{-4}% of thymol[55].

With increased acidity of the solution, the rate of disproportionation of uranium(V) increases too, which in turn raises the rate of regeneration of uranium(VI) and hence the height of the first wave. This is confirmed by the decrease of the height of the first reduction wave for hexavalent uranium in the presence of tetravalent uranium, which reduces the rate of disproportionation of pentavalent uranium[53]. On the other hand, when precipitants and complex-forming agents for tetravalent uranium are added, the height of the wave increases as a result of the disproportionation of pentavalent uranium[60]. When the acidity of the solution is above 5 *N*, the wave becomes irreversible[60] owing to the elimination of oxygen atoms from the uranyl ion in the bulk of the solution[70]. One should note that the proportionality of the height of the first wave to the concentration of hexavalent uranium holds only in the acidity range 0.01−0.1 *N* and at higher acidities the height increases faster than the concentration of uranium(VI).[53-55] Thus the final product of the electrode reaction corresponding to the first main wave may be either tetravalent uranium or a mixture of tetravalent and pentavalent uranium (the literature data on this question are ambiguous).

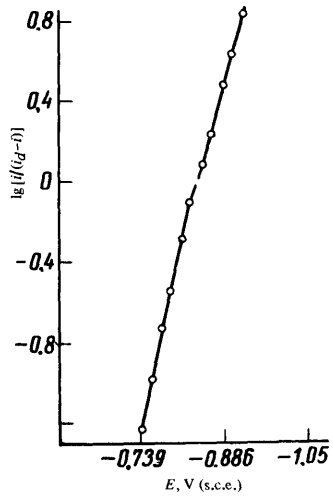


Figure 2. Analysis of the second wave for the reduction of uranium(VI) in 10^{-3} M $UO_2(ClO_4)_2$ + 0.1 M $HClO_4$ solution[59].

In aqueous chloride and perchlorate solutions of uranium(VI), the second main wave, observed in the potential range between −0.7 and −1.2 V (s.c.e.), is believed[53-67] to be due to the postulated limiting degree of reduction of uranium to the tervalent state. It is noteworthy that there is no generally accepted explanation of the nature of the second uranium(VI) wave, since it corresponds to the reduction of uranium to a valence state which has not been determined unambiguously. Thus, many investigators[53,61] believe that the wave corresponds to the reduction of pentavalent uranium to the tervalent state, while others[56,57] explain it by the reduction of a mixture of pentavalent and tetravalent uranium ions to the tervalent state. Some workers[59] think that in a hydrochloric acid solution (>0.1 *N*) the second main wave is associated with the reduction of only tetravalent uranium to the tervalent state owing to the high rate of disproportionation of pentavalent uranium. The plot of E against $\lg[i/(i_d - i)]$ corresponding to this wave has a break[53] or even a discontinuity[59], which indicates the complexity of the electrode process corresponding to the wave (Fig. 2). The height of the second wave is equal to that of the first when the acidity of the solution is about 0.1 *N*; on the other hand, with increase of the acidity above this value, the height of the second wave increases and in 6 *N* HCl is twice as high as that of the first wave, which, as stated above, also increases somewhat[60]. The increased heights of both uranium(VI) waves with increasing acidity of the solution can be accounted for by the fact that they correspond not only to the reduction of uranium but also to the catalytic

† Relative to the saturated calomel electrode.

discharge of hydrogen ions. One should note that kinetic data on the disproportionation of pentavalent uranium are necessary for an unambiguous explanation of the nature of both the second and first wave. However, the literature on this question does not meet this requirement (the most reliable method for the investigation of this reaction is at present the polarography of hexavalent uranium itself[71,72]).

At pH 2—3.5, in solutions free from complex-forming agents, the second uranium(VI) wave splits into two steps with half-wave potentials of −0.85 and −1.15 V (s.c.e.).[55,57,59,61]. There is no generally accepted explanation in the literature of the reasons for this phenomenon. For example, some workers[55,57] explain it in the following way. At a high pH, part of the hexavalent uranium or its reduction products form electrochemically indifferent deposits on the mercury cathode which rules out the possibility of quantitative reduction of uranium to the final (for aqueous solutions) tervalent state. On the other hand, starting from pH 2—3.5, the deposits dissolve. The low rate of this process is responsible for the marked kinetic arrest of the reduction of uranium in the deposits, which is in turn responsible for the appearance of the additional step on the second wave. However, the dissolution of uranium deposits in solutions at pH 2—3.5 rules out the possibility of their formation, so that the above explanation of the causes of the splitting of the second uranium wave fails. We believe that the reason for the separation of the second uranium(VI) wave into two steps is as follows. The pH range in which this phenomenon is observed coincides with the range where pentavalent uranium is most stable according to a number of reports[64-67]. According to some data[73], in this pH range the rate of disproportionation falls so much that the concentration of pentavalent uranium in solution can reach 10^{-3} M. Therefore, in the pH range 2—3.5, there is not sufficient time for the disproportionation reaction to convert pentavalent uranium fully into the hexavalent and tetravalent forms. The residual pentavalent uranium is reduced at potentials which are intermediate between those for the reduction of hexavalent and tetravalent uranium[74] and its reduction appears as a separate stage.

Additional data concerning the nature of the second uranium(VI) wave are provided by the results of certain studies on the polarography of tetravalent uranium. In particular the upper step on the second uranium(VI) wave has the same half-wave potential as the cathodic wave of tetravalent uranium[54,57,59]. This confirms the above hypothesis that in the pH range 2—3.5 hexavalent uranium is not reduced quantitatively to the tetravalent state because in the potential range of the second wave, corresponding to the reduction of uranium to the tervalent state, an additional wave, corresponding to the reduction of pentavalent uranium to the tetravalent state, appears.

As stated above, the limiting degree of reduction of hexavalent uranium in aqueous solutions at a mercury electrode is generally believed[50-56,59-69] to correspond to the tervalent state. However according to one report[57], in 0.1 N HCl a third wave with a half-wave potential of approximately −1.60 V (s.c.e.), corresponding in the author's view to the reduction of tervalent uranium to the metal, was observed together with the two principal uranium(VI) waves described above. This wave is largely masked by the hydrogen wave[57] and subsequently could not be reproduced even in special investigations[62].

Thus, in acid aqueous solutions free from complex-forming agents, uranium(VI) is reduced at a mercury electrode to the pentavalent state at potentials between −0.12 and −0.28 V (s.c.e.) and is then converted into the tetravalent form owing to the high rate of disproportionation. At potentials between −0.65 and −1.2 V (s.c.e.), tetravalent uranium is reduced to the tervalent state. Owing to a lower rate of disproportionation in solutions at pH 2—3.5, the reduction of pentavalent uranium takes place partly as a separate stage at potentials close to the reduction potential of uranium(IV).

Partial replacement of water by organic solvents does not have a significant influence on the electrochemical behaviour of uranium at a mercury electrode. In particular, as in aqueous solutions, uranium(VI) is reduced to the final tervalent state in two main stages[75-86].

The electrochemical behaviour of uranium at a mercury electrode in aqueous solutions containing complex-forming agents differs from that in chloride and perchlorate solutions. Thus, depending on the stability of the complexes, the primary effect is a widening of the pH range in which polarography of uranium is possible. In addition, there is a change in the very nature of its polarograms.

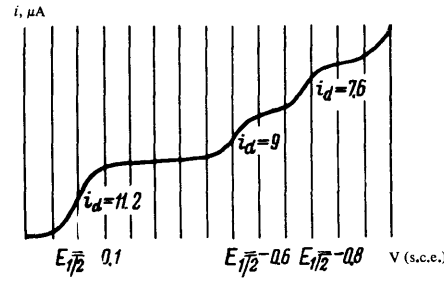


Figure 3. Polarogram for the reduction of uranium(VI) in 1.9×10^{-3} M UO_2SO_4 + 0.025 N H_2SO_4 + 0.1 N Na_2SO_4 solution[61].

In those cases where weak complex-forming agents are present in solution, for example sulphate ions {hexavalent uranium forms the sulphate complex[23] $[UO_2(SO_4)_2]^{2-}$ with $K_{inst} = 1.4 \times 10^{-3}$}, the maximum pH at which polarography of uranium is possible reaches 6—7; on the other hand, the principal characteristics of the behaviour of uranium at a mercury electrode remain the same[57,61,87-91]. In particular, in sulphate solutions, as in chloride and perchlorate solutions, two main waves are observed, the second of which corresponds to the reduction of uranium to the tervalent state[57,61,87-91] (Fig. 3). Compared with chloride and perchlorate solutions, the splitting of the second uranium(VI) waves into two steps in sulphate solutions is observed over a wider pH range (0—7) [89] (in chloride and perchlorate solutions the corresponding pH range is 2—3.5). With increase of acidity from 0.01 to 1.0 N (at a constant hexavalent uranium concentration), the height of the first wave increases and that of the lower step of the second wave falls, but their sum remains constant[88]. A number of investigators[61,88,89] believe that the reason for the splitting of the second wave into two steps in sulphate solutions is a lower rate of disproportionation of pentavalent uranium owing to its complex formation, i.e. the lower step of the second wave corresponds to the reduction of pentavalent uranium and the upper step to the reduction of tetravalent uranium to the final tervalent state.

In solutions of other weak complex forming agents, for example acetates, the following uranium(VI) complexes are known: $[UO_2Ac]^+$, $[UO_2Ac_2]$, and $[UO_2Ac_3]^-$ with $K_{inst} = 2.3 \times 10^{-3}$, 2.2×10^{-5}, and 5.7×10^{-7} respectively[23]; the electrochemical behaviour of uranium(VI) in such solutions does not differ significantly from its behaviour in sulphate solutions. Thus in uranium(VI) acetate solutions two main waves are observed as in solutions of its simple salts. Many investigators believe[54,55,92-96] that the first wave in their experimental pH range (2.5—6) corresponds to reversible one-electron reduction of uranium(VI) to the pentavalent state. On the other hand, the second wave corresponds to the irreversible reduction of pentavalent uranium to the tervalent state[92-96]. It should be noted that the somewhat higher stability of uranium acetate complexes compared with the sulphate complexes suppresses the disproportionation of pentavalent uranium to such an extent that the polarographic pattern is not complicated by the partial conversion of uranium into the tetravalent form in the first stage of the reduction of hexavalent uranium. As with solutions of simple uranium(VI) salts, the second wave splits into two steps at pH 3 [55,93] or at pH 5.[94,95] With increase in the concentration of acetate ions from 0.004 to 0.2 M (at a uranium concentration of 10^{-3} M), the half-wave potential for the second stage of the reduction of uranium(VI) shifts from −0.18 to −0.40 V (s.c.e.) without an appreciable change in the height of the wave[94]. Under the same conditions, the overall height of the second wave, observed at potentials of about 1 V (s.c.e.) falls to a value which is no longer susceptible to measurement[94]. Many investigators explain the splitting of the second uranium(VI) wave into two steps by the retardation of the disproportionation of pentavalent uranium in acetate solutions owing to its binding into acetate complexes[93,94]. It is difficult to agree with this explanation. Indeed, the independence of the height of the first wave of acetate ion concentration shows that the disproportionation of uranium(V) is slow in such solutions and therefore the second wave corresponds to the reduction of pentavalent uranium. We believe that the reason for the splitting of the second uranium(VI) wave into two steps is the considerable difference between the compositions and stabilities of uranium(V) and uranium(IV) acetate complexes {the complexes $[UO_2Ac]$ with $K_{inst} = 2.6 \times 10^{-2}$ and $[UOAc_2]$ with $K_{inst} = 2.4 \times 10^{-6}$ have been suggested for uranium(V) and uranium(IV) [93] respectively}. This means that at high acetate ion concentrations the reduction of uranium(V) to the tetravalent state takes place as a separate stage of the overall electrode process corresponding to the reduction of uranium(V) to the tervalent state. On the other hand, the decrease of the overall height of the second uranium(VI) wave with increase of the concentration of acetate ions can be accounted for by the formation of negatively charged uranium(V) acetate complexes, which are reduced at the negatively charged surface of the mercury electrode with a marked kinetic arrest.

Thus, in the presence of weak complex-forming agents the electrochemical behaviour of uranium(VI) at a mercury electrode does not differ significantly from its behaviour in solutions of its simple salts. On the other hand, in the presence of powerful complex-forming agents, the electrochemical behaviour of uranium differs sharply from that in its simple salt solutions or solutions containing weak complex-forming agents. It is then greatly influenced by the differences between the stabilities of complexes of uranium in different valence states. For example, in uranium(VI) carbonate solutions (pH > 10), owing to the low stability of the uranium(IV) carbonate complex (the composition of which has not established exactly[23,97]) and probably also the uranium(V) complex, only one wave is observed in the range of potentials between −0.9 and 1.20 V (s.c.e.); according to a number of investigators[55,97-106], this corresponds to the reduction of uranium(VI) to uranium(V), which is converted into the final (under these conditions) tetravalent state as a result of disproportionation.

In the pH range 8—10, yet another weak wave is observed in carbonate solutions[97,103-105]; the authors state that it arises because part of the tetravalent uranium is not involved in disproportionation owing to the formation of its hydroxide and is reduced to the tetravalent state (the lowest possible under these conditions) at more negative potentials, ranging from −1.2 to −1.4 V (s.c.e.). The absence of this wave in carbonate solutions at pH > 10 is explained by some workers[104,105] by the high rate of formation of a uranium dioxide deposit, which in turn accelerates the disproportionation of pentavalent uranium. In connection with the foregoing, studies on the electrolysis of uranium(VI) carbonate solutions at a mercury macrocathode are of definite interest. In particular, after the electrolysis of these solutions at pH 8—10, tetravalent uranium was detected, in addition to uranium(VI), both in solution and in the form of a uranium dioxide precipitate[104,105]. It has been reported[104] that under these conditions the solutions contain appreciable amounts of uranium(V), which is doubtful owing to the high rate of its disproportionation.

Uranium in different valence states forms complexes with ethylenediaminetetra-acetic acid (EDTA), the stabilities of which differ markedly. However, in contrast to carbonate solutions, in EDTA solutions uranium(IV) and not uranium(VI) complexes are the more stable[107-109]. Data on the polarography of uranium(VI) in EDTA solutions are not unambiguous. Thus, according to some results[95,110-113], obtained by the method of classical polarography, only one wave is observed for solutions containing EDTA. The half-wave potential for this process is independent of uranium(VI) and EDTA concentrations, but, when the pH is changed from 3 to 7, it shifts from −0.35 to −0.45 V (s.c.e.).[112,113] The height of this wave at pH 3—5 is proportional to the concentration of uranium(VI). However, with increase of pH at a constant uranium(VI) concentration, it diminishes and at pH > 7 merges with the wave of the supporting electrolyte[112]. The reason for this effect is a decrease of the concentration of uranium(VI) owing to its precipitation (in EDTA solutions at pH > 7.5, hexavalent uranium is precipitated quantitatively as the diuranate[107-109,112,113]).

According to other data[113] obtained by oscillographic polarography, two cathodic peaks corresponding to one-electron processes are observed in the same solutions at high rates of application of potential. The same investigators showed that, at relatively low rates of application of potential, the height of the first peak decreases with increasing pH, which they believe to be due to the limited rate of disproportionation of uranium(V). They state that in uranium(IV) solutions in the presence of EDTA cathodic peaks are not observed.

We believe that, despite a certain ambiguity of the polarographic data for uranium in EDTA solutions, they lead to the conclusion that, owing to the high stability of the uranium(IV) complex in such solutions, the rate of disproportionation of uranium(V) is also high and for this reason the final product of even the first stage in the

reduction of uranium(VI) is not only pentavalent but also tetravalent uranium.

The elucidation of the causes responsible for the absence of the wave corresponding to the reduction of uranium(IV) in solutions of hexavalent or tetravalent uranium containing EDTA is of definite interest. One of the possible causes may be a pronounced kinetic arrest of the reduction of uranium(IV) due to the formation of a negatively charged complex with EDTA. It has been found[112,113] that in this complex the ratio U^{IV} : EDTA = 1 : 1. This implies that uranium(IV) must enter into this complex in the ionic form UO^{2+}. Moreover, other investigators suggested[107-109] that, depending on the pH and the excess EDTA present, uranium(IV) enters into complexes in different ionic forms and that the molar ratio of EDTA and uranium in such complexes may exceed unity. The reasons for the absence of the uranium(IV) reduction wave may be also a high negative potential of the U^{IV}/U^{III} system due to the fact that the uranium(IV) complex of EDTA is much more stable than the corresponding uranium(III) complex. The lack of unambiguous data on the composition of uranium(IV) complexes of EDTA and also data on the stabilities of the possible uranium(III) complexes of EDTA precludes at the moment an unambiguous conclusion concerning this problem.

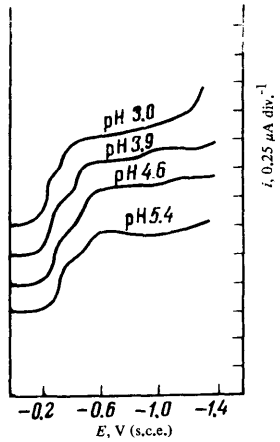


Figure 4. Polarogram for the reduction of uranium(VI) in 2×10^{-4} M $UO_2(NO_3)_2$ + 0.1 M H_3Cit + 0.1 M KCl solution containing 2.6×10^{-4}% of gelatine[117].

In solutions containing complex-forming agents which bind uranium in stable complexes in all its valence states, its electrochemical behaviour differs sharply from that in all the cases discussed above. For example, uranium(VI) forms the citrate complex[114] $[UO_2cit]^-$ with $K_{inst} = 2 \times 10^{-9}$, while according to other data[115,116] uranium(IV) forms compounds in which the citrate ion : uranium ratio varies from unity to two. The polarograms for the reduction of uranium(VI) in citrate solutions show two principal waves[63,117] (Fig. 4) as for the solutions of its simple salts. Thus at a pH of about 2, the corresponding half-wave potentials are −0.21 and −0.90 V (s.c.e.).[117] In the pH range 3—5, the first waves splits into two steps[117]. (Owing to the inhibition of the disproportionation of pentavalent uranium, in chloride and perchlorate solutions the second wave consists of two steps.) It is believed[117] that splitting of the first wave is due to inhibition of the disproportionation of uranium(V) caused by the formation of its complexes with citrate ions, as a result of which the reduction of pentavalent uranium to the tetravalent state takes place as an independent stage. With increase of the pH of the citrate solution from 3 to 5, the half-wave potentials for the two steps of the first wave shift towards negative values by approximately 30 and 20 mV respectively (until they completely merge); on the other hand, the sum of their heights remains constant[117]. Thus the first uranium(VI) wave in citrate solutions corresponds to its reduction to the tetravalent state.

With increase of the pH of the citrate solution from 3 to 5, the height of the second wave decreases until it merges completely with the wave of the supporting electrolyte[117]. The above investigators acknowledge that the nature of the second wave is ill-defined, since, according to their data for citrate solutions of uranium(IV), no waves are observed under these conditions[117]. We believe that this inconsistency is due to the appreciable difference between the composition of the uranium(IV) citrate complex prepared by mixing solutions of its simple salt and of the complex-forming agent and the composition of the uranium(IV) citrate complex obtained from the uranium(VI) complex as a result of a rapid electrode reaction, i.e. in the polarography of the uranium(VI) citrate complex the electrode process corresponding to the first wave results in the formation of an intermediate form of the uranium(IV) citrate complex which does not have sufficient time during the recording of the polarogram for conversion into the final electrochemically passive state.

Thus in citrate solutions uranium(VI) is reduced to the tervalent state in two stages. At pH 3—5, the first stage in the reduction of uranium(VI) to the tetravalent state also involves two stages.

Additional data on the electrochemical behaviour of uranium at a mercury electrode have been provided by oscillographic and cyclic polarographic studies and also by an investigation of the electrochemical oxidation of uranium in lower valence states at mercury and platinum electrodes. In particular, the results of these studies demonstrate that, depending on the composition of the solutions and their pH, two- and three-stage reduction of uranium(VI) to the tervalent state takes place at a dropping mercury electrode; the potentials of the cathodic peaks occur under these conditions in the ranges where the corresponding waves are observed on the classical polarograms for the reduction of uranium(VI).[113,118-125] However, whereas in the case of classical polarography the reduction of pentavalent uranium occurs as a separate stage only in solutions of specific composition, in oscillographic polarographic studies this stage in the reduction of uranium is observed when the rate of application of potential to the dropping mercury electrode is increased[118-125].

Together with the reduction of the higher valence forms of uranium, its lower valence forms are oxidised irreversibly at the dropping mercury electrode (the oscillographic polarograms show anodic peaks which are appreciably lower than the corresponding cathodic peaks and are displaced towards positive potentials relative to the latter)[121,125]. It is noteworthy that the relatively low heights of the anodic peaks compared with those of the cathodic peaks may be caused not only by the irreversibility of the anodic processes but also by diffusion of part of

the reduced uranium, obtained in the cathodic polarisation of the electrode, from the layer near the electrode into the bulk of the solution. Moreover, as shown above, the reduction of uranium at a mercury electrode should be accompanied by the catalytic discharge of hydrogen ions, which increases the heights of the cathodic peaks.

Polarographic data on the anodic oxidation of uranium(IV) are ambiguous. Thus it has been stated[59,125,126] that the oxidation of uranium(IV) takes place not only at a platinum electrode but also at a mercury electrode, while, according to another report[57], the oxidation of uranium(IV) is not observed even at platinum electrode potentials reaching +0.45 V (s.c.e.).

It is noteworthy that quantitative characteristics of the uranium reduction and oxidation processes at a mercury electrode have not yet been obtained from oscillographic polarographic data. The reason for this is the inadequacy of the theoretical interpretation of the experimental data. For example, in studies on the reduction of uranium(VI) [120] and the oxidation of lower valence forms of uranium[119,121], the processes were interpreted quantitatively (i.e. the diffusion coefficients, activation energies, and transfer coefficients were calculated) on the basis of the experimental data in terms of a theory developed for another case[127-129]. Indeed this theory is concerned with electrode processes involving substances diffusing from the solution to the surface of the electrode (and not conversely as in the oxidation of the lower valence forms of uranium obtained on the electrode during its brief cathodic polarisation in a hexavalent uranium solution[119,121]). Moreover, the theory does not provide for the possible disproportionation of the reduction products of the test substances.

A wave associated with the oxidation of uranium amalgam to uranium(IV) has been reported[130,131]. However, the results of this study and also their explanation are not sufficiently convincing, since the wave is observed in 1 *N* H_2SO_4 at potentials of −1.42 [130] or −1.52 [131] V (s.c.e.) (beyond the hydrogen wave), i.e. more negative than the potentials at which uranium(IV) is reduced reversibly to the tervalent state[53-55,59,61]. Moreover, according to another report[34], when uranium amalgam comes into contact with aqueous solutions it is oxidised to uranium(III), which is clearly detected.

As already stated, the height of the first wave for the reduction of uranium(VI) in chloride and perchlorate solutions, observed in the potential range from −0.1 to −0.25 V (s.c.e.), is proportional to its concentration in the range 10^{-5}—10^{-3} M when the acidity is between 0.01 and 0.1 *N*. In certain cases this can have analytical applications. However, the narrow range of acidities in which polarographic determination of uranium in solutions of its simple salts is possible involves a number of disadvantages. In the presence of even weak complex-forming agents, for example sulphate ions, the range of permissible acidities of the solution analysed extends to 0.01—2.5 *N*.[10,23] The use of more powerful complex-forming agents permits the determination of uranium in neutral and even alkaline solutions[23]. The complex dependence of the height of the second wave for the reduction of uranium(VI) on solution composition rules out its employment for analytical purposes. The available methods for the polarographic determination of uranium require the preliminary separation of a number of impurities which are reduced at potentials corresponding to the first wave of uranium(VI). Therefore these methods for the determination of uranium in most cases cannot compete with other available procedures, for example spectrophotometric techniques[23]. At the present time the polarographic method is mainly used for the remote monitoring of the concentration of uranium solutions in certain technological processes[10,23].

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Kirov Kazakh State
University, Alma-Ata

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The Hydrogen Bond in Sulphur-containing Compounds

I.V.Zuika and Yu.A.Bankovskii

The contemporary state of the problem of the proton-donating ability of the mercapto-group and the proton-accepting ability of a sulphur atom in sulphur-containing compounds in the formation of a hydrogen bond is described. The effect of the hydrogen bond on various physicochemical properties of sulphur-containing compounds is examined. A comparison is also made of the ability of sulphur-containing compounds and their oxygen-containing analogues to form a hydrogen bond. 306 references.

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I. INTRODUCTION

Several reviews have already appeared[1-9] which deal with the general problems of the hydrogen bond (HB) X–H←Y, its properties in various classes of compounds, and methods of investigation. The bulk of the information relates to HB of the types O–H←O, O–H←N, and N–H←O. The ability of the mercapto-group and a sulphur atom to form HB, that is, HB of the types S–H←Y, or X–H←S (where Y = O, N, S, F, Cl, or Br; X = O or N) has not been reviewed and all the information on this problem that has accumulated is scattered in individual papers.

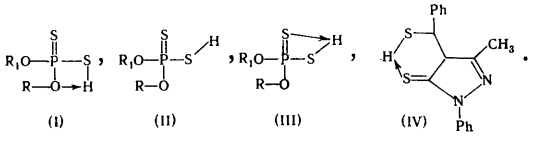
The present article reviews the available (including 1970) information on the HB S–H←Y and X–H←S (X and Y = O, N, or S) in various classes of organic compounds.

II. PROTON-DONATING ABILITY OF THE MERCAPTO-GROUP IN ORGANIC COMPOUNDS IN THE FORMATION OF HYDROGEN BONDS (S–H←S, S–H←O, S–H←N, S–H←Hal)

1. The S–H←S Hydrogen Bond

The ability of aliphatic and aromatic mercaptans to form S–H←S HB was questionable for a long time. Despite extensive investigations of various physicochemical properties of thiols[10-33] the opinion persisted until the 'fifties' that autoassociation in such systems did not exist.

In 1956, on the basis of the splitting of the ν_{SH} band in the infrared spectra of solutions of *o,o'*-diethyl and *o,o'*-dimethyldithiophosphoric acids [presumably *OO*-diethyl and *OO*-dimethyl *S*-hydrogen phosphorothiolothionates (Ed. of Translation)] in CCl_4, Menefee and coworkers[34] postulated the autoassociation of the molecules of these compounds by means of an S–H←S HB. The same type of association is assumed in dithiophosphoric[35,36], diphenyldithiophosphinic[37] [diphenylphosphinodithioic? (Ed. of Translation)], and dithiobenzoic[35] acids. However, recent cryoscopic studies showed that the dithiophosphoric acids [*S*-hydrogen phosphorothiolothionates (Ed. of Translation)] exist as monomers in benzene solution[38]. The observed splitting of the ν_{SH} bands in the vibrational spectra of the dialkyl *S*-hydrogen phosphorothiolothionates (~ 2550 and 2590 cm^{-1})[38-43] is explained by the existence of rotational isomers with an S–H←O intramolecular hydrogen bond (IHB) (I) between the SH group and an ester oxygen[38,42,43]. The band in the higher frequency region (~ 2590 cm^{-1}) evidently corresponds to the rotational isomer with a free SH group (II) and not the isomer with the S–H←S IHB (III)[42]:



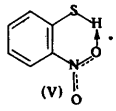
In the dithiobenzoic acid molecule (dilute solutions in cyclohexane) Issleib and Grundler[44] postulate chelation by a direct S–H←S IHB, which is responsible for the appearance of two energetically non-equivalent $n \rightarrow \pi^*$ transitions in the CSS group. The presence of an S–H←S IHB is also responsible for the absence of a concentration dependence of the ν_{SH} frequency of the ν_{SH} vibrations (2400 cm^{-1}) in the infrared spectra of solutions of 4-mercapto-3-methyl-1-phenylbenzylidene-5-thiopyrazole (IV) in CCl_4.[45] The association of ethylene trithiocarbonate [1,3-dithiolan-2-thione (Ed. of Translation)] and of thiofenchone with thiophenol, *p*-thiocresol, *p*-chlorothiophenol, *p*-bromothiophenol, and butane-1-thiol by means of an S–H←S HB is accompanied by a blue shift of the $n-\pi^*$ absorption band of the thiocarbonyl group.[46,47]

On the basis of the splitting of the ν_{SH} band in the infrared spectra (2580 and 2560 cm^{-1}), Spurr and Byers[48] established the ability of aliphatic thiols and thiophenol to undergo autoassociation by means of an S–H←S HB. Splitting of the ν_{SH} absorption band due to an S–H←S HB was also observed in the infrared spectra of solutions of *p*-chlorothiophenol (2583 and 2569 cm^{-1}) and *p*-methylthiophenol (2584 and 2571 cm^{-1}) in CCl_4.[49] Other results obtained as a result of investigations of the infrared and NMR spectra of thiophenol[49-54], the infrared spectra of the halogen derivatives of thiophenol[52], the NMR spectra of *o*- and *m*-methylthiophenols[55], the infrared and NMR spectra of aliphatic thiols[53,54,56-62], the infrared spectra of dithiocarbamic acid[63], and the NMR spectra of sulphanes

H_2S_x ($x = 1-9$),[64] also confirm the ability of thiols to undergo autoassociation by means of an S–H←S HB. The NMR spectra suggest that an S–H←S IHB exists in the H_2S_3 molecule[64]. Crystallographic results show the existence of an S–H←S HB in hydrogen sulphide[65]. The formation of dimers and trimers of hydrogen sulphide (matrix-isolated in solid nitrogen) was also proved recently by infrared spectroscopy[60].

2. S–H←O and S–H←N Hydrogen Bonds

According to results obtained in studying physicochemical properties in solutions of thiols in proton-withdrawing solvents associates are formed by means of S–H←O and S–H←N intermolecular HB[15,67-72], and this is also confirmed, despite various objections[29,33,73,74], by the results of spectroscopic investigations. Cleveland and coworkers[75] observed splitting of the ν_{SH} band (2536 and 2569 cm^{-1}) in the Raman spectra of solutions of thiophenol in dioxan, and this is attributable to an S–H←O HB. This is confirmed by the results of investigations of the association of thiophenol with dioxan and acetone by infrared spectroscopy[51]. Gragerov and Pogorelyi[76] determined the energies of the S–H←O HB of the associates of thiophenol, its derivatives, and thio-2-naphthol with acetone. A similar splitting of the ν_{SH} band is observed in the infrared spectra of solutions of thiophenol in diethyl, ethyl phenyl, and diphenyl sulphoxide[77] and of *p*-nitrophenol and *o*-nitrophenol in CCl_4.[78] Chelation by an S–H←O_2N IHB is presumed for *o*-nitrophenol (V). The S–H←O_2N HB leads to splitting of both $\nu_S(NO_2)$ and $\nu_{AS}(NO_2)$ absorption bands[78]. As was noted in Section II.1, an S–H←O IHB also exists in alkyl dithiophosphoric acids:



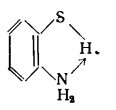
(V)

The association of thiophenol, *p*-nitrothiophenol, and *o*-nitrothiophenol with dioxan by an S–H←O HB is also accompanied by some increase in the dipole moment of these thiols in comparison with the dipole moment measured in benzene (Table 1).

It has been shown that the rate of proton exchange is increased in proportion to the strength of the S–H←O HB of the associates of thiophenol or its derivatives with acetone[79].

The ability of thiophenol to associate with proton-withdrawing solvents by an HB was shown in several NMR studies[46,80-82], and by infrared[83,84], and ultraviolet[46] spectroscopy. A similar type of interaction with proton-withdrawing solvents is also effected for methanethiol, propane-1-thiol, and hydrogen sulphide[56,85-87]. Table 2 gives the equilibrium constant (K_{26}) at 26°C and the energy ($-\Delta H$) of the S–H←Y HB (Y = O or N) for some 1 : 1 associates of thiophenol with proton-withdrawing solvents.

A thorough investigation of the ability of *o*-amino- and *o*-hydroxy-thiophenol to form an HB was made by David and Hallam[49]. Evidently, in *o*-aminothiophenol in CCl_4 there is an S–H←N IHB (VI)[49,88], although the dipole moment in benzene does not agree with the *cis*-configuration[89]:



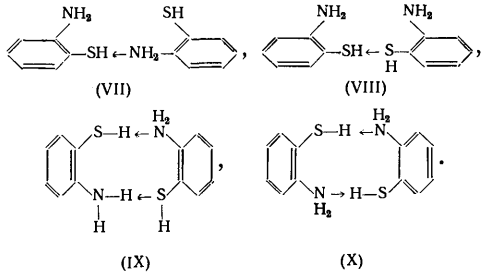
(VI)

However, it must be borne in mind that the S–H←N IHB may be destroyed with the formation of associates of benzene-*o*-aminothiophenol.

Table 1. Dipole moments of thiophenol and of its derivatives in benzene (B) and dioxan (D).[78]

Compound	μ_B, D	μ_D, D	$\Delta\mu_i=\mu_D-\mu_B$
C_6H_5SH	1.19—1.23	1.28	0.10—0.06
o-$NO_2C_6H_4SH$	4.69	4.81	0.12
p-$NO_2C_6H_4SH$	3.77	4.07	0.30

In concentrated solutions in CCl_4 *o*-aminothiophenol exists as dimers of open (VII or VIII) or cyclic (IX or X) structure[49]:



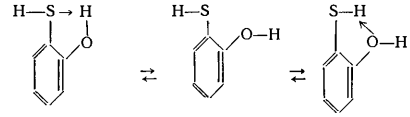
(VII) (VIII)

(IX) (X)

Table 2. Equilibrium constants and energies of the HB of thiophenol–proton-withdrawing solvent associates.

Solvent	K_{26}, litre $mole^{-1}$	$-\Delta H$, kcal $mole^{-1}$	Reference
Acetone	0.29	3.2	76
Pyridine	0.22	2.4	81
N-Methylpyrazole	0.14	2.1	81
Tributyl phosphate	0.43	2.0	81
Dimethylformamide	0.24	1.8	81
Benzene	0.04	0.5	81
N-Methylacetamide	—	0.9	80

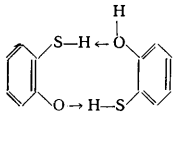
The complex relation between concentration and the frequencies and intensities of the ν_{OH} and ν_{SH} bands in the infrared spectra of solutions of *o*-hydroxythiophenol in CCl_4 is due to the formation of a different type of HB between the OH and SH groups. As the concentration is raised the IHB of (XIa) and (XIb) are broken and dimers of *o*-hydroxythiophenol are formed (XIc) and (XId).



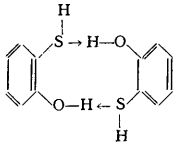
(XIa) (XI) (XIb)

$\nu_{(S-H)}$ 2595 cm^{-1} 2595 cm^{-1} 2547 cm^{-1}

$\nu_{(O-H)}$ 3463 cm^{-1} 3606 cm^{-1} 3606 cm^{-1}



(XIc)
ν(S—H) 2535 cm^{-1}
ν(O—H) 3606 cm^{-1}



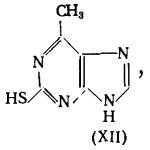
(XId)
2595 cm^{-1}
3463 cm^{-1}

The ability of 5-mercaptoquinoline to form associates by means of an S–H···Y HB is seen from the decrease in the frequency of the ν_{SH} band in benzene compared with that in carbon tetrachloride ($\Delta\nu$ = 21 cm^{-1}) and the increase in the dipole moment on going from benzene to dioxan as solvent ($\Delta\mu_1$ = 0.28D).[90-92]

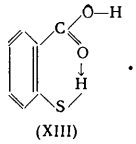
The previously expressed hypothesis of the absence of association in aliphatic aminothiols[33] was disproved by an investigation of the infrared spectra of solutions of aminothiols of the general formula $R_{3-n}N(CH_2CH_2SH)_n$ in CCl_4.[93] The splitting of the ν_{SH} band (2620 and 2560 cm^{-1}) in these systems is due to an S–H···N hydrogen HB. The autoassociation energy for various aminothiols $R_{3-n}N(CH_2CH_2SH)_n$ varies from 1.9 to 2.5 kcal mole^{-1} (calculated from $\Delta\nu$).

On the basis of spectroscopic results, the absence of association in thiocarboxylic acids RCOSH by means of a HB has been noted repeatedly[32,35,94,95]. However, thioacetic acid can evidently undergo this type of interaction in the liquid phase[96]. Recently published results confirm this opinion: as a result of autoassociation by an S–H···O HB both the $\nu_{C=O}$ and ν_{SH} absorption bands of thioacetic and thiobenzoic acids are split[97].

X-ray diffraction and neutron diffraction results show the possibility of the existence of an S–H···O HB in crystalline 2-mercapto-6-methylpurine (XII)[98]:



(XII)

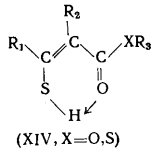


(XIII)

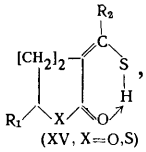
Chelation in the thiosalicylic acid molecule is effected by an S–H···O IHB (XIII), as a result of which the $\nu_{C=O}$ absorption band in the infrared spectra is split (1718 and 1730 cm^{-1}).[99]

The energy of the IHB in thiosalicylic acid is 0.9 kcal mole^{-1}. The presence of S–H···O IHB has been established in β-thioketoesters (XIV; X = O)[100-103], β-thioketothiol esters (XIV; X = S)[104-107], α-thioacyl-lactones (XV, XVI, XVII; X = O) and α-thioacylthiol-lactones (XV, XVIII; X = S)[108], monothio-β-diketones (XIX)[100,109-113], and the β-mercaptoamide of cinnamic acid (XXI)[106,114] by NMR methods and by infrared and ultraviolet spectroscopy.

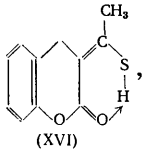
Chelation of the S···H–O type (XX) in monothio-β-diketones has been suggested[115,116-119], but has not yet been proved satisfactorily[100]. Chelation by an S–H···O IHB was also found in 1-mercaptoanthraquinone (XXII)[120], thioglycollic acid (XXIIIa) and (XXIIIb)[121], and dimercaptopropenones (XXIV)[122]:



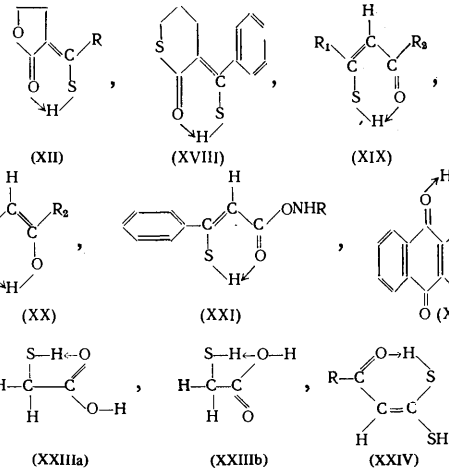
(XIV, X=O,S)



(XV, X=O,S)



(XVI)



(XII) (XVIII) (XIX)

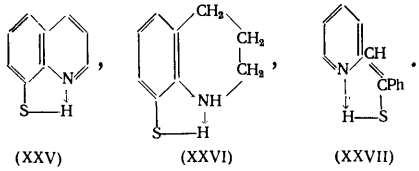
(XX) (XXI) (XXII)

(XXIIIa) (XXIIIb) (XXIV)

The anomalously low frequency of the $\nu_{C=O}$ vibrations (1560 cm^{-1}) in dimercaptopropenones is due to the formation of a six-membered quasiaromatic ring (XXIV), which according to Shigorin[123] leads to the strongest IHB in oxygen-containing compounds.

Use of infrared spectroscopy and dipole moments enables us[91,92,124-126] to establish the existence of 8-mercaptoquinoline, its methyl and halogeno-derivatives in solutions and in the liquid phase in the *cis*-configuration with an S–H···N IHB (XXV), which confirmed the earlier assumption of chelation in the molecules of 8-mercaptoquinoline[127,128] and its 2-methyl derivative[129]. $-\Delta H$ of the S–H···N IHB is 2.4–3.2 kcal mole^{-1} for various 8-mercaptoquinoline derivatives. In polar organic solvents the S–H···N IHB in these compounds is not destroyed with the formation of associates having a direct intermolecular HB S–H···Y.

The 1,2,3,4-tetrahydro-8-mercaptoquinoline molecule also contains a ring with an S–H···N IHB (XXVI), the energy of which is 1.5 kcal mole^{-1}.[130] However, unlike 8-mercaptoquinoline, in this instance autoassociates are formed by means of S–H···S or S–H···N HB and also associates with proton-withdrawing solvents by means of S–H···Y HB. The strength of the S–H···N IHB being higher in 8-mercaptoquinoline than in 1,2,3,4-tetrahydro-8-mercaptoquinoline is due to the different hybridisations of the nitrogen atoms in these compounds[125]. According to the infrared spectra, there is an S–H···N IHB in phenyl 2-picolyl thioketone (XXVII)[131]:



(XXV) (XXVI) (XXVII)

3. The S–H···Hal Hydrogen Bond

Little information about the S–H···Hal HB is available. The assumption, based on measurements of the dipole moment, of the existence of *o*-chlorothiophenol and *o*-bromothiophenol in the *cis*-configuration with an S–H···Hal IHB[78] agrees well with the wavenumbers of the ν_{SH} vibrations (2552 and 2545 cm^{-1}, respectively), being appreciably lower than that for thiophenol (2587 cm^{-1})[52].

The infrared spectra and dipole moments suggest that chelation by an S–H⋯Hal IHB is also achieved in 6-fluoro-, 6-chloro-, and 6-bromo-5-mercaptoquinoline, and in 7-fluoro-, 7-chloro-, and 7-bromo-8-mercaptoquinoline[90,92,125]. The strength of the S–H⋯Hal IHB in these compounds increases from the bromo- to the fluoro-derivative.

III. PROTON-WITHDRAWING ABILITY OF A SULPHUR ATOM IN ORGANIC AND INORGANIC COMPOUNDS IN THE FORMATION OF HYDROGEN BONDS (O–H⋯S, N–H⋯S, C–H⋯S)

1. O–H⋯S and N–H⋯S Hydrogen Bonds

Owing to the presence of unshared electron pairs, sulphur atoms in organic compounds can participate in the formation of HB also as an acceptor of a proton (that is, a donor of electrons), and in particular this is confirmed by the existence of S–H⋯S HB in aliphatic and aromatic thiols (see Section II).

Table 3. Blue shift of the n-π^* band of the C=S group, association constant, and energy of the S→H–O HB of ETTC–proton-donating solvent associates.

Solvent	pK_{OH} (Refs.46, 135 & 136)	σ^*(Ref.137)	ETTC		
			K_{26}, litre mole^{-1} (Ref.132)	$-\Delta H$, kcal mole^{-1} (Ref.133)	$\Delta\nu(n\rightarrow\pi^*)$, cm^{-1} (Ref.46)
H_2O	7.05	—	—	6.5	—
CH_3OH	15.50	0.000	—	2.4	825
C_2H_5OH	15.93	−0.100	0.286	2.0	705
n-C_3H_7OH	16.10	−0.115	0.245	—	—
n-C_4H_9OH	16.10	−0.130	0.198	—	—
iso-C_3H_7OH	17.10	−0.190	0.137	1.9	585
t-C_4H_9OH	19.20	−0.300	0.038	1.7	585
$C_6H_5CH_2OH$	15.40	+0.215	0.620	—	—
$CF_3HCF_2CH_2OH$	12.74	+0.600	—	—	2404
CF_3CH_2OH	12.40	+0.920	—	—	2275
$CHCl_3$	—	—	—	1.9	—

A reliable criterion of the formation of associates by compounds which contain a thiocarbonyl group, by means of a C=S→H–X HB is thought to be the blue shift of the absorption band of this group. The assumption of the formation of a C=S→H–O HB on the basis of this effect between ethylene trithiocarbonate [1,3-dithiolan-2-thione (Ed. of Translation)] (ETTC, XXVIII) and alcohols[46,132,133] agrees completely with the infrared spectra for the ETTC-(proton-donating solvent) systems[134]. The blue shift of the $n\rightarrow\pi^*$ band of the thiocarbonyl group, the association constant at 26°C,[132] and $-\Delta H$ of the C=S→H–O HB of the ETTC–(proton-donating solvent) associates[133] are given in Table 3. This shows a distinct correlation between K_{26} and the acidic properties (pK_{OH}), that is, with the proton-donating properties of the alcohols, which is characterised by the inductive constant of the hydrocarbon radical of the alcohol (σ^*).

A tendency is also noted for an increase in the blue shift of the n-π^* band of the C=S group with increase in the proton-donating ability of the molecule in various alcohols (Tables 3 and 4) and phenols (Table 5). However, a similar correlation between the proton-donating ability (pK_a or σ^*) of the compounds of various classes (alcohols, phenols) and the blue shift of the band of the C=S group (ETTC) is not observed.

Table 4. Blue shift of the n-π^* band of the C=S group in alcohols[46].

Compound	$\Delta\nu(n\rightarrow\pi^*)$, cm^{-1}			
	CH_3OH	C_2H_5OH	iso-C_3H_7OH	t-C_4H_9OH
Thiazolidinethione	2100	1770	1600	1600
ETTC	825	705	585	585
Thiofenchone	430	440	300	270

Recently, the absence of a correlation between $-\Delta H$ of the C=S→H–O HB of ETTC–(phenols or acid derivatives of phenols) associates was also reported[138]. However, the reliability of the results and the conclusions of this work[138] are doubtful—for example, $\Delta\nu(n$-$\pi^*)$ is the same for solutions of ETTC in phenol, p-chlorophenol, and m-cresol. There are many published examples which show that for compounds of a single type RX–H (where X = O or S) there is a distinct correlation between their acidic properties and spectral ones and also the thermodynamic characteristics of the RX–H–Y HB with the same proton acceptor Y (Tables 3–6 and Section IV).

Table 5. Blue shift of the n-π^* band of the C=S group of ETTC in the phenols (R = C_6H_4OH).[46]

R	σ	pK_{OH}	$\Delta\nu(n\rightarrow\pi^*)$, cm^{-1}
p-Cl	0.23	9.38	1020
H	0.00	9.95	390
p-CH_3	−0.17	10.19	380
p-OCH_3	−0.27	10.20	235

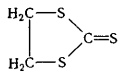
We have observed a clear correlation between the proton-donating ability of normal aliphatic alcohols and $-\Delta H$ of the S^-→H–O HB of the associates of zwitter-ion form (8-mercaptoquinoline, 5-mercaptoquinoline, and their derivatives)—alcohol (Table 6)[139-142].

The decrease in $-\Delta H$ for the S^-→H–O HB for 8-mercaptoquinoline as compared with that of 5-mercaptoquinoline is due to the presence of an S^-→H–N IHB in the molecule of the former[141,142].

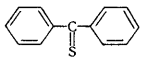
The blue shift of the n-π^* band of the C=S group for solutions of thiobenzophenone (XXIX) in ethanol[143,144], methyl (XXX; R = CH_3) and isopropyl thiocarbamates (XXX; R = Pr^i), thiocamphor (XXXI), ETTC (XXVIII) in phenol[145], alkylthioureas (XXXII) in phenol and ethanol[146], and 2-mercaptobenzothiazole (LIX) in acetic acid[147] are also due to C=S→H–O HB.

The association of alkylthioureas and thiocamphor with phenol by S→H–O HB[146,148,149] is also confirmed by the shift of the ν_{OH} band of phenol to lower frequencies. A similar type of interaction is also observed for the association of phenol with N≡CSN$(CH_3)_2$.[150] $-\Delta H$ of the

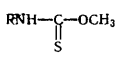
S→H–O HB for some of these systems are given in Table 7.



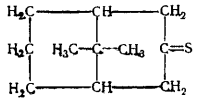
(XXVIII)



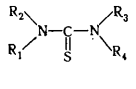
(XXIX)



(XXX)



(XXXI)



(XXXII)

Table 6. Energy of the S⁻→H–O HB of associates of the zwitter-ion form of 8-mercaptoquinoline (R), of its methyl derivatives (CH_3–R), and of 5-mercaptoquinoline (R_1) with aliphatic alcohols.

Solvent	σ*	−ΔH, kcal mole⁻¹					
		R	2CH_3–R	4CH_3–R	6CH_3–R	7CH_3–R	R_1
CH_3OH	0.000	1.40	1.45	2.17	1.56	1.52	2.00
C_2H_5OH	0.100	0.80	0.85	1.56	0.90	0.86	1.60
n-C_3H_7OH	0.115	0.76	0.70	1.45	0.82	0.75	1.54
n-C_4H_9OH	0.130	0.73	0.65	1.26	0.71	0.65	1.50

The energies of the S→H–O HB of the associates of thiocamphor with propanol and tetrafluoropropanol are 1.8 kcal mole^{-1} ($\Delta\nu_{OH}$ = 120 cm^{-1}) and 3.6 kcal mole^{-1} ($\Delta\nu_{OH}$ = 170 cm^{-1}) respectively[46].

X-ray diffraction studies show a strong S→H–O HB exists in the crystalline 6-thiopurine riboside hydrate[151] and sodium *NN*-diethyldithiocarbamate trihydrate[152]. There is also a similar interaction in crystalline monohydrates of bis(isoquinoline-1-carboxaldehyde thiosemicarbasonato)nickel[153], 6-mercaptopurine[154,155], potassium[156] and caesium[157] trithiocarbonates, and barium thiosulphate[158].

Table 7. Energy of the HB (−ΔH) between compounds containing a thiocarbonyl group and phenol.

Compound	−ΔH, kcal mole⁻¹	Reference	Compound	−ΔH, kcal mole⁻¹	Reference
Alkylthiourea	4—4.8	146	Thiocamphor	5.0	145
Thiocarbamates	4.0	145	Ethylenetrithiocarbonate (ETTC)	3.2	145

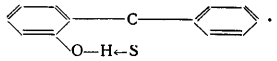
Spectroscopic investigation of the interaction of sulphides with proton-withdrawing solvents shows that in these systems association is also effected by means of S→H–O HB. The splitting of the ν_{OH} band in the infrared spectra of the *p*-chlorophenol–sulphide[159,160], phenol–sulphide[160,166], and phenol–aryl sulphide[167] systems is due to excitation of the OH group of the S→H–O HB with sulphide sulphur (Table 8).

The values[162,164] of −ΔH of the S–H→O HB of dibutyl sulphide–phenol and diethyl sulphide–phenol associates (Table 8) are evidently somewhat too high. According to Table 8, −ΔH of the S→H–O HB is greater in these instances than for associates of the corresponding sulphides with *p*-chlorophenol. However, bearing in mind the higher acidic properties of *p*-chlorophenol (pK_{OH} = 9.38[168]) compared with those for phenol (pK_{OH} = 9.98[169]) a strengthening of the S→H–O HB on going from phenol to *p*-chlorophenol can be postulated. The higher stability of the *p*-chlorophenol–sulphide associates compared with that of the sulphide–phenol associates is also shown by the greater shift of the ν_{OH} band to lower frequencies in the first instance. Δν and −ΔH vary symbathically for monotypical compounds[1], which is observed, for example, for the tetrahydrothiopyran–phenol and tetrahydrothiopyran–*p*-chlorophenol systems (Table 8). Consequently, the value of −ΔH = 3.40 kcal mole^{-1} [163] for associates diethyl sulphide–phenol is more probable than −ΔH = 4.60 kcal mole^{-1}.[164]

Table 8. Displacement of the ν_{OH} band and energy of the S→H–O HB of phenol and *p*-chlorophenol with the sulphides.

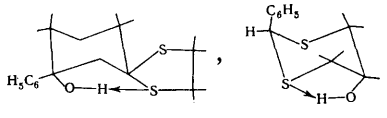
Compound	Phenol				*p*-Chlorophenol			
	Δν, cm^{-1}	reference	−ΔH, kcal mole^{-1}	reference	Δν, cm^{-1}	reference	−ΔH, kcal mole^{-1}	reference
Dibutyl sulphide	254	162	4.26	162	280	159	3.7	159
Diethyl sulphide	250	161	4.60	164	274	159	3.5	159
Ditto	210	163	3.40	163	—		—	
Methyl phenyl sulphide	170	161	3.40	161	—		—	
Ethyl propyl sulphide	—		—		276	159	3.7	159
Ethylene sulphide	210	160	2.38	160	—		—	
Propylene sulphide	222	160	2.42	160	—		—	
Trimethylene sulphide	248	160	2.91	160	—		—	
Tetrahydrothiopyran	244	160	2.99	160	282	159	3.9	159
Tetrahydrothiophen	262	160	3.39	160	—		—	

On the basis of the spatial position of the functional groups in 2-hydroxythiobenzophenone the formation of an S→H–O HB can be postulated (XXXIII), which evidently explains the absence of a blue shift for the n–π^* absorption band in proton-donating solvents (ethanol)[170]:



(XXXIII)

Finding the presence of an S→H–X IHB is often used in conformational analysis. Mertes[171,172] attributes the absorption at 3446 cm^{-1} (according to Szmant and Rigau[173], at 3500 cm^{-1}) and 3478 cm^{-1} in the infrared spectra of phenylmercaptoindanol (XXXIV) and 5-hydroxy-2-phenyl-1,3-dithione (XXXV) to the ν_{OH} vibrations of the *cis*-configuration, with an excited S→H–O IHB:

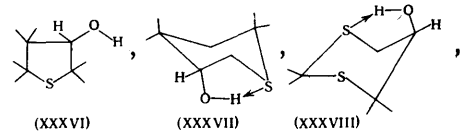


(XXXIV) (XXXV)

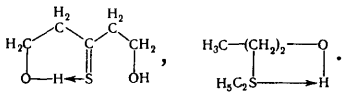
According to Szmant and Rigau, −ΔH of the S→H–O IHB in (XXXIV) is 2.5 kcal mole^{-1}.[173]

The shift of the ν_{OH} band to lower frequencies owing to the formation of an S→H–O type of IHB was also observed in the infrared spectra of thiocyclopentan-3-ol (XXXVI),[174] some of its derivatives[175], thiocyclohexanol (XXXVII),[174]

1,3-dithiocyclohexan-5-ol (XXXVIII),[174] its 2-phenyl derivative[176], 3-thiopentane-1,5-diol (XXXIX),[177] ω-ethylmercaptoalkanols (XL)[165,178], 2,2'-thiodiphenol[179], its derivatives[180], 2,2'-thiobis-(3,4,6-trichlorophenol), and 2,2'-thiobis-(4,6-dichlorophenol)[179]:

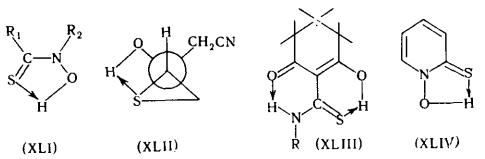


(XXXVI) (XXXVII) (XXXVIII)

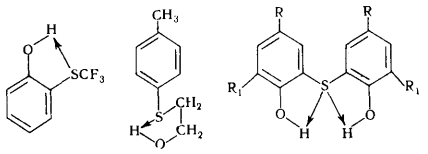


(XXXIX) (XL)

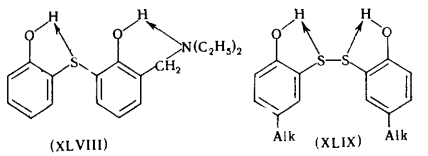
Chelation by S→H–O HB was also found in *o*-methylthiophenol, 2-methyl-6-methylthiophenol, *o*-isopropylthiophenol[181,182,183], thioacetylhydroxamic acid (XLI)[184], 1-cyano-3,4-epithio-2-hydroxybutane (XLII)[185] by NMR and infrared spectroscopy, in 4,4-dimethyl-2,6-dioxothiocyclohexanecarboxanilide (XLIII)[186], in monothio-β-diketones (XX)[115] by the NMR method, in 1-hydroxy-2-thiopyridone (XLIV)[188], and *o*-trifluoromethylphenol (XLV)[183] by infrared spectroscopy and in compounds of the (XLVI)–(L) type by dipole moments and infrared spectroscopy[180,188,189] and NMR[190,191].



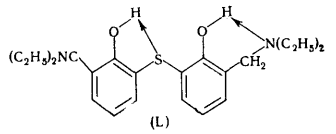
(XLI) (XLII) (XLIII) (XLIV)



(XLV) (XLVI) (XLVII)



(XLVIII) (XLIX)

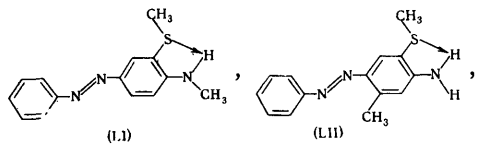


(L)

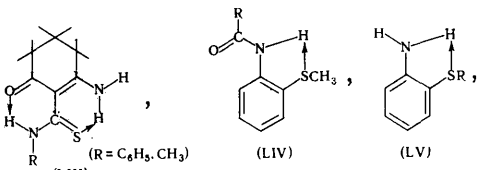
However, the problem of the presence of an S→H–O IHB in (XLVII) (when R_1 = H, CH_3), and also in XLVIII and XLIX) evidently cannot be regarded as settled. According to the results of recent investigations it seems that an S→H–O IHB can be formed only in the compounds (XLVII) with a sufficiently bulky substituent R_1 (t-butyl etc.).[190]

It is also noteworthy that the assumption of the presence of an S→H–O IHB in compounds (XX) based on the appearance in the NMR spectra of the signal of an OH group does not agree with the results of various other investigations[100,109-113] (section II.2).

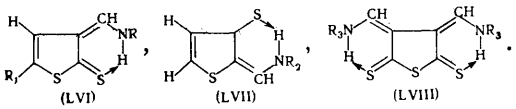
Chelation by means of an S→H–N type IHB has been established on the basis of the ν_{NH} band in the infrared spectra in dimetoate [sic. the compounds referred to in Ref. 192 are *o*-methylthio-derivatives of *N*-methylaniline and *N*-methyl-4-aminoazobenzene (Ed. of Translation)][192] and in compounds (LI) and (LII)[193], and by NMR spectroscopy in compounds (LIII)[186] and (LIV)[194]. NMR and infrared spectroscopy show that an S→H–N IHB exists in *o*-aminothiophenols (LV)[195] and mercaptoaldimines of the thiophene series (LVI)–(LVIII)[196,197]:



(LI) (LII)

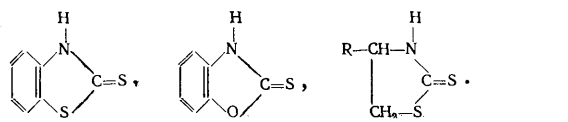


(LIII) (R = C_6H_5, CH_3) (LIV) (LV)



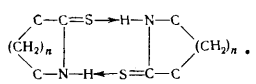
(LVI) (LVII) (LVIII)

Association by an HB of S→H–N type was first proved by Hopkins and Hunter[71] on the basis of cryoscopic measurements of the molecular weights of thioamides. This was later confirmed spectroscopically[198-204]. The broad band in the infrared spectra of 2-mercaptobenzothiazole (LIX), 2-mercaptobenzoxazole (LX), 2-mercaptothiazoline (LXI; R = H), and 2-mercapto-4-methylthiazole (R = CH_3) at 3050 cm^{-1} is due to the ν_{NH} vibrations of the associated molecules by the S→H–N HB[198]:



(LIX) (LX) (LXI) (R = H, CH_3)

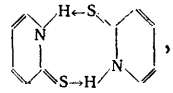
The proton-withdrawing ability of the thiocarbonyl group of these compounds in the formation of HB is confirmed by the blue shift of the n–π^* band of the C=S group for solutions of 2-mercaptobenzothiazole in proton-donating solvents[147]. According to Kulevsky and Froehlich[205], the splitting of the ν_{NH} band in the infrared spectra of solutions of thiolactams in benzene is due to the formation of dimers of structure (LXII):



(LXII)

The value of $-\Delta H$ of the S→H–N HB of thiobutyrolactam is 5.8 kcal $mole^{-1}$, that of thiovalerolactam 3.1 kcal $mole^{-1}$, and that of thiocaprolactam 3.3 kcal $mole^{-1}$. A similar conclusion was reached[206] concerning the autoassociation of thiocaprolactam in benzene from the infrared spectra and dipole moments. The dimerisation of (LXII) leads to a considerable decrease in μ (2.78 D) in comparison with μ of the monomer (4.59 D). It is necessary to note the considerable discrepancy in the values of the dimerisation constants for thiocaprolactam

(K_D = 370 litre mole^{-1} [205] and K_D = 93 litre mole^{-1} [206]) is noteworthy. K_D = 370 litre mole^{-1} is evidently too high if it is taken into account that for caprolactam K_D = 270 litre mole^{-1} and $-\Delta H$ for the O→H–N HB of the caprolactam dimers is 5.5 kcal mole^{-1}. [206] Cryoscopic [207,208] and dielectric [209] measurements and also investigation of the infrared spectra [187] showed that 2-thiopyridone in benzene and chloroform is dimerised like thiocaprolactams by the S→H–N HB (LXIII):



(LXIII)

The dimerisation of 2-thiopyridone in benzene leads, as for thiocaprolactam, to a considerable decrease in μ (2.78 D) in comparison with μ of the monomer (5.26 D for the *N*-methyl derivative). The dimers of thiocaprolactam and 2-thiopyridone are destroyed in dioxan [207, 208].

The infrared spectra show the association of *N*-methylaniline with thiocamphor by an S→H–N HB, the energy of which is 5.7 kcal mole^{-1}. [46]

Intermolecular association by means of an S→H–N HB is also effected in the sulphide–thiocyanic acid system (Table 9). [209]

Table 9. Displacement of the ν_{NH} band and $-\Delta H$ for the S→H–N HB of thiocyanic acid with sulphides [209].

Solvent	$\Delta\nu$, cm^{-1}	$-\Delta H$, kcal mole^{-1}	Solvent	$\Delta\nu$, cm^{-1}	$-\Delta H$, kcal mole^{-1}
Dimethyl sulphide	380	3.48	Di-t-butyl sulphide	440	4.48
Ethyl methyl sulphide	390	3.47	Tetrahydrothiapyran	400	3.69
Diethyl sulphide	400	3.49	Tetrahydrothiophen	420	3.62
Di-n-butyl sulphide	400	3.59	Trimethylene sulphide	383	3.28

It is suggested that the anti-swelling action of 6-thioguanine [210] is due to the formation of an S→H–N HB between the sulphur atom in this analogue of guanine and the amino-group of cytosine, which is situated opposite the sulphur atom in DNA [211]. An analogous interaction is also assumed between the thiocarbonyl group of thionicotinamide and the amino-group of adenine in the sulphur-containing analogue of dihydrophosphopyridine nucleotide [212].

The formation of an S→H–N HB in crystals has been discussed [213–215]. In crystalline 2-mercaptobenzothiazole there is a considerable decrease in the N...S distance (2.48 Å) in comparison with the N...S distance due to the van der Waals interaction associated with the S→H–N HB [216]. Penfold [217] assumes the presence of an S→H–N HB in crystalline 2-thiopyridone, the strength of which is considerably less than in crystalline 2-mercaptobenzothiazole (the N...S distance in 2-thiopyridone is 3.26 Å). On the basis of crystallographic results (Table 10) an analogous type of intermolecular interaction can be assumed in crystalline ammonium diamidothiophosphate [218], diammonium amidothiophosphate [219], thiosemicarbazide [220–222], pyridazo-3-thione [213,223], 3-hydroxy-5-thio-1,2,4-thiazole [224], thioacetamide [225], 1-thiocarbamylimidazoline-2-thione [226], 2,5-diamino-4-mercapto-6-methylpyrimidine [227], xanthene hydride [228], triethylenediaminecadmium(II) thiosulphate [229], 3-ethoxy-2-ketobutyraldehyde bis(thiosemicarbazone) [230], 2,4-dithiouranyl [231], the thiourea–parabanic acid (oxalylurea) complex [232], 2-propyl-4-thiocarbamoylpyridine [233], 4-thiocarbamoylpyridine [234], 4-formylpyridine thiosemicarbazone [235], 2-formylthiophen thiosemicarbazone [236], thiocytosine [237], copper ammonium thiomolybdate [238], 2,2′-diaminodiphenyl disulphide [239], thiocarbohydrazide [240], dithio-oxamide [241], 2-mercapto-6-methylpurine [98], 1,2,4-trithiolane-3,5-dione [242], 6-thioguanine [243], thiourea [244,245], trimethylenethiourea [246], allylthiourea [247], and also (despite certain objections [248]) in ethylenethiourea [1].

Table 10. N...S intermolecular distance.

Distance, A	Compound	Reference
3.366	pyridaz-3-thione	213,223
2.48	2-mercaptobenzothiazole	216
3.26	2-thiopyridone	217
3.400—3.484	ammonium diamidothiophosphate	218
3.312—3.478	diammonium amidothiophosphate	219
3.34; 3.39, 3.359; 3.409	thiosemicarbazide	220 221,222
3.24	3-hydroxy-5-thiol-1,2,4-triazole	224
3.396—3.504	thioacetamide	225
3.40	1-thiocarbamoylimidazolidine-2-thione	226
3.40	2,5-diamino-4-mercapto-6-methylpyrimidine	227
3.35	xanthene hydride	228
2.75; 2.93	triethylenediaminecadmothiosulphate	229
3.32—3.54	bis(thiosemicarbazone)-3-ethoxy-2-keto-butyraldehyde	230
3.315; 3.335	2,4-dithiouracyl	231
3.312	thiourea–parabanic acid	232
3.39	2-propyl-4-thiocarbamoylpyridine	233
3.44	4-thiocarbamoylpyridine	234
3.496	4-formylpyridine thiosemicarbazone	235
3.348; 3.360	2-formylthiophen thiosemicarbazone	236
3.34	thiocytosine	237
3.48	copper–ammonium thiomolybdate	238
3.48; 2.29; 2.67	2,2′-diaminodiphenyl disulphide	239
3.406	thiocarbohydrazide	240
3.43; 3.46	dithio-oxamide	241
3.37	2-mercapto-6-methylpyrin	98
3.60	1,2,4-trithiolan-3,5-dione	242
3.327; 3.303	6-thioguanine	243
3.35—3.43	thiourea	244,245
3.31	trimethylenethiourea	246
3.36	allylthiourea	247
3.44	ethylenethiourea	1

The existence of an S→H–N HB in crystalline thiourea and its tertiary derivatives was also shown by infrared spectroscopy [249,250].

2. The S→H–C Hydrogen Bond

The possibility of the formation of an HB of S→H–C type has also been noted. Engberts [251] recently suggested, on the basis of NMR results, such interaction between α-diazosulphones (RSO_2CHN_2) and thiophen. According to Bellamy and Rogasch [134], the association of chloroform with ETTC is assumed to be by an S→H–C HB. The ability of chloroform to form S→H–C HB with 8-mercaptoquinoline, its derivatives, their zwitter-ion forms, and aliphatic thiols has been postulated [56,125,141,252]. An analogous interaction, judging by interatomic distances, can evidently be presumed in crystalline 2,4-dithiouracyl [231], thiocarbamoyl-4-pyridine [234] and ethionamide [ethyl-2-thiocarbamoyl-4-pyridine] [253].

However, owing to the lack of experimental results the problem of an S→H–C type of HB still remains open.

IV. COMPARISON OF THE ABILITIES OF SULPHUR- AND OXYGEN-CONTAINING COMPOUNDS TO FORM HYDROGEN BONDS

The proton-donating ability of the X–H group in the formation of X–H···Y HB is usually linked with the acidic properties of the compounds RX–H (where X, Y = O or S)[251-262]. As the acidic properties of X–H increase there is an increase in the strength of the X–H···Y HB with the same acceptor of a proton. This correlation is also observed in the series of thiophenol derivatives[263] (Table 11). From this point of view a tendency (greater than for the hydroxyl group) for the mercapto-group to undergo association with the same proton-withdrawing molecule is to be expected. However, in reality on comparing proton-donating molecules with which the atom X (X–H) is situated in different Periods of the Mendeleev system, there is not a proportionality between the ability of the X–H group to act as a proton donor in the formation of an HB and its strength as an acid. For example, for the hydrohalogen acids the acidic properties of which decrease in the order HI > HBr > HCl > HF, the energy of the HB with the same proton-withdrawing molecule changes in the reverse order[264,265].

Table 11. Frequency characteristics of the ν_{SH} band of thiophenol and of its *p*-substituted derivatives in proton-withdrawing solvents.

Substituent	pK_a	CCl_4		Benzene		Acetonitrile		Acetone	
		ν_{SH}	$\Delta\nu$	ν_{SH}	$\Delta\nu$	ν_{SH}	$\Delta\nu$	ν_{SH}	$\Delta\nu$
NH_2	9.7	2559	0	2551	3.1	2547	4.7	2541	7.0
OCH_3	8.8	2572	0	2565	2.7	2561	4.3	2548	9.3
H	8.3	2590	0	2574	6.2	2565	9.7	2558	12.4
Cl	7.3	2588	0	2567	8.1	2557	12.0	2544	17.0
NO_2	5.8	2589	0	2562	10.4	2547	16.2	2519	27.0

An analogous effect is also observed for compounds which contain SH and OH groups. Compounds which contain an SH group always exhibit more acidic properties than their hydroxyl-containing analogues. However, under strictly equal conditions compounds of the RSH type form a less stable HB than compounds of the ROH type. For example, thiophenol (pK_{SH} = 6.5 [266]) forms less stable HB than phenol (pK_{OH} = 9.98 [169]) with proton-withdrawing solvents (Table 12).

An analogous effect is also observed for autoassociation of phenol and thiophenol, for which $10^2\Delta\nu/\nu$ (the relative displacement of the maximum of the ν_{XH} band in the formation of an HB) is 3.4 [273] and 0.73 [49] respectively. The effect of the S–H···O_2N IHB in *o*-nitrothiophenol on the displacement of the $\nu_s(NO_2)$ and $\nu_{as}(NO_2)$ bands ($10^2\Delta\nu/\nu$ = 1.54) is also considerably less than for the O–H···O_2N IHB of *o*-nitrophenol ($10^2\Delta\nu/\nu$ = 9.6 [78]). Several studies have shown that the rate of exchange of the protons in SH groups is several orders of magnitude less than in OH groups, which is the result of the strength of the S–H···S HB being less than that of the O–H···O HB.[76,274,275] The lesser ability of the mercapto-group to form HB is also confirmed by the lower association constants of aliphatic thiols compared with those of aliphatic alcohols (Table 13).

This agrees well with the investigation of chelation in thiosalicylic acid[99] and 8-mercaptoquinoline[125]. The energy of the S–H···O IHB in thiosalicylic acid ($-\Delta H$ = 0.9 kcal mole^{-1}) is considerably less than the O–H···O IHB in salicylic acid ($-\Delta H$ = 5 kcal mole^{-1} [278,279]) despite the lower acidity of the latter.

Table 12. Spectroscopic and thermodynamic characteristics of hydrogen bonds formed by thiophenol and phenol with proton-withdrawing solvents.

Proton acceptor	Thiophenol					Phenol				
	$10^{-2}\frac{\Delta\nu}{\nu}$	A, litre cm^{-2} mole^{-1}	K_{26}, litre mole^{-1}	$-\Delta H$, kcal mole^{-1}	reference	$10^{-2}\frac{\Delta\nu}{\nu}$	A, litre cm^{-2} mole^{-1}	K_{26}, litre mole^{-1}	$-\Delta H$, kcal mole^{-1}	reference
Pyridine	4.45	—	0.22	2.4	44,81	12.9	—	77	6.0	263,267
								42	6.5	45
Dimethylformamide	—	—	0.24	1.8	44,81	6.3	—	70	6.1	268
	—	—	—	—	—	—	—	64	—	46
Dioxan	1.43	—	—	—	44	6.85	3.34	4.1	5.5	269,270
Acetone	0.97	—	—	—	44,76	6.5	—	—	—	263
Tetrahydrofuran	2.5	0.68	—	—	78	8.3	3.49	—	5.7	269
Benzene	0.81	0.35	0.039	0.5	78,81	1.32	0.97	0.37	1.56	269,271
	—	—	—	—	—	—	—	0.20	1.60	46
Diethyl sulphoxide	3.75	—	—	—	77	10.0	—	—	—	77
Ethyl phenyl sulphoxide	2.70	—	—	—	77	9.5	—	—	—	77
Diphenyl sulphoxide	1.85	—	—	—	77	8.3	—	—	—	77
Dibutyl ether	0.73	—	—	—	32	7.5	—	—	—	269,272

The strength of the S–H···N IHB in 8-mercaptoquinoline ($-\Delta H$ = ~ 3 kcal mole^{-1}) is much less than that of the O–H···N IHB in 8-hydroxyquinoline ($-\Delta H$ = ~ 6 kcal mole^{-1}).[125] The acidic properties of 8-mercaptoquinoline (pK_{SH} = 8.48 [280]) greatly exceed those of 8-hydroxyquinoline (pK_{OH} = 9.89 [281]).

Table 13. Association constants (K) of aliphatic alcohols and thiols.

Substance	K, litre mole^{-1}	Reference	Substance	K, litre mole^{-1}	Reference
Ethanol	0.64	276	Ethanethiol	0.021	48
n-Propanol	0.89	277	Propane-1-thiol	0.052	48
n-Butanol	0.78	277	Butane-1-thiol	0.016	48

The experimentally observed inverse relationship between the ability of the mercapto- and hydroxyl groups to form HB and their acidic properties is due to the difference in the nature of the S–H and O–H chemical bonds.

From the point of view of the covalent nature of the X–H···Y HB[282,283], the existence of a definite relation between the proton-donating ability of the X–H group and the tendency of the H atom of this group to receive electrons of atom Y is postulated[284]. Evidently two mechanisms of the transfer of electrons to the H atom are possible: to the vacant (antibonding[250,260-285]) orbital X–H or to the 1*s* orbital of the bonded H atom[283,286] with use therein of its residual overlap capability. The latter should increase with decrease in the *S*-integral for the overlap of the X–H bond[287]. The value of the *S*-integral

depends on the nature of the remaining part of the molecule (R) and the electronegativity (EN) of the atom X. With increase in the inductive nature of R and in the EN of atom X there is a decrease in the probability of the residence of the electrons in the overlap region which reduces S and increases the proton-donating ability of X–H. Consequently, the strength of the X–H···Y HB for a given donor of electrons Y depends on the degree of "protonisation" of the hydrogen atom[288]. For the same atom X the degree of "protonisation" and the acidic properties of the molecule due to the influence of the radical R on the X–H bond are symbatic to one another.

Table 14. Dipole moments of 2-thiopyridone, 2-pyridone, and their *N*-methyl derivatives in dioxan (μ_D).[208]

Compound	μ_D, D
2-Pyridone	2.94
N-Methylpyrid-2-one	4.07
2-Thiopyridone;	5.29
N-Methyl-2-thiopyridone	5.49

In comparing proton-donating molecules which contain different atoms X it is also necessary to take into account differences in the value of the *S* overlap integral[289]. For many compounds the proton-donating ability of the X–H group correlates well with the EN of atom X[289] and also with the size of the electron cloud (with the principal quantum number of the valence electrons of atom X[99,288,290]). These correlations are evidently a reflection of relation between the proton-donating ability and *S* already mentioned[289], since *S* is a function of both the difference in EN and the dimensions of the atoms being bonded[291,292]. Correlation of the proton-donating ability of the X–H groups with the EN of the atoms X is observed when there is a considerable difference in EN or when the sizes of atoms X are similar. When the atoms X have similar EN the sizes of the electron clouds must be considered (for example, N–H and Cl–H or C–H and I–H)[289].

In compounds with an S–H group, as compared with their oxygen analogues, the valence orbitals of the sulphur atom are much more delocalised in space than those of the oxygen atom. This is connected with the greater principal quantum number of the valence electrons of the sulphur atom. Because of this the *S* overlap integral of the S–H bond is considerably greater than that of the O–H bond. In accordance with this, an increase in the *S* integral leads to a decrease in the "protonisation" of the H atom, that is, to a decrease in the proton-donating ability of the S–H group and consequently to a decrease in the strength of the S–H···Y HB in comparison with the strength of the O–H···Y HB. However, the S–H bond is considerably weaker than the O–H bond, owing to the greater delocalisation in space of the valence orbitals of the sulphur atom, compared with those of the oxygen atom. The lower energy of the bonding of the hydrogen atom in the S–H group is a reason for the higher acidity of the compounds with an S–H group compared with those of their oxygen analogues. Consequently, replacement of an oxygen atom by a sulphur atom in the X–H group (X = O or S) brings about, on the one hand, a decrease in the degree of "protonisation" of the hydrogen atom, leading to a weakening of the HB with the proton-withdrawing molecule, and, on the other, to the loosening of the X–H bond, increasing its ability for ionisation.

A comparison of the proton-withdrawing capability of sulphur and oxygen atoms in the formation of HB is also of interest.

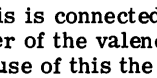
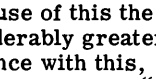
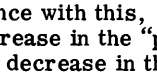
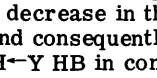
2-Thiopyridone (Section III) is dimerised[208] in solutions in benzene, as also is 2-pyridone[208]. According to measurements of the dipole moments of 2-thiopyridone, 2-pyridone, and their *N*-methyl derivatives, the dimers of 2-thiopyridone (unlike 2-pyridone) are broken down in solutions (Table 14).

Table 15. $\Delta\nu_{OH}$ and $-\Delta H$ of the O–H···Y HB of $(C_4H_9)_2Y$–C_6H_5OH associates[162].

Y	$\Delta\nu_{OH}$, cm^{-1}	$-\Delta H$, kcal mole^{-1}
O	278	5.98
S	254	4.26
Se	210	3.72

According to results obtained in an investigation of $(C_4H_9)_2Y$–C_6H_5OH associates (Y = O, S, Se) the energy of the O–H···Y HB and the displacement of the ν_{OH} band to lower frequencies decreases in the order O > S > Se (Table 15).

Table 16. Displacement of the ν_{OH} band, association constant (K_{20}), and energy of formation of the associates ($-\Delta H$) of ethers and thioethers with phenol and its derivatives.

Compound	Y	Phenol (Refs.160 & 163)			*p*-Chlorophenol (Ref.159)		
		$\Delta\nu$, cm^{-1}	K_{20}, litre mole^{-1}	$-\Delta H$, kcal mole^{-1}	$\Delta\nu$, cm^{-1}	K_{20}, litre mole^{-1}	$-\Delta H$, kcal mole^{-1}
$(C_4H_9)_2Y$	O	—	—	5.71	305	13.6	5.4
	S	—	—	4.19	280	3.2	3.7
$C_2H_5YC_3H_7$	O	—	—	—	300	16.2	5.3
	S	—	—	—	276	3.4	3.7
$(C_2H_5)_2Y$	O	270	9.6	4.6	300	12.1	5.0
	S	165	4.7	3.4	274	3.0	3.5
	O	290	9.36	4.32	—	—	—
	S	244	1.38	2.99	—	—	—
	O	295	9.83	4.25	316	34.5	5.8
	S	262	2.49	3.39	282	8.3	3.9
	O	299	13.3	4.97	—	—	—
	S	248	1.37	2.91	—	—	—
	O	220	5.95	3.75	—	—	—
	S	222	1.08	2.42	—	—	—

Investigations of the interaction of the esters and thioesters triethyl phosphate and triethyl phosphorothioate with proton-donating solvents (phenol and its derivatives) also showed that the strength of the O–H···Y HB formed by sulphur-containing compounds (Y = S) is much less than that for their oxygen-containing analogues (Y = O) (Tables 16 and 17).

For IHB an analogous relation between the strengths of the O–H⋯S and O–H⋯O HB was shown by examples of ω-ethylmercaptoalkanol and ω-methoxyalkanol[178]. The high strength of the O–H⋯S IHB compared with that of the O–H⋯O IHB in five-membered rings[181,183,184] is an exception. It seems that in five-membered rings the N–H⋯S IHB is also much stronger than the N–H⋯O.[195] This is explained by the sulphur atom being larger than the oxygen atom, which leads to a greater overlap of the orbitals having a lone pair with the 1*s* orbital of the hydrogen atom being greater for sulphur.

Table 17. Displacement of the ν_{OH} band, association constant (K_{20}), and energy of formation of the associates ($-\Delta H$) of triethyl phosphate and triethylthiophosphorothionate with phenol and pentachlorophenol[163].

Compound	Y	Phenol			Pentachlorophenol		
		Δν, cm^{-1}	K_{20}, litre $mole^{-1}$	$-\Delta H$, kcal $mole^{-1}$	Δν, cm^{-1}	K_{20}, litre $mole^{-1}$	$-\Delta H$, kcal $mole^{-1}$
$(C_2H_5O)_3P=Y$	O	345	350,5	6.7	481.1	153.1	5.2
	S	172	4.5	3.2	202	2.9	3.3

In the literature the proton-withdrawing ability of a molecule in the formation of an X–H⋯Y HB is usually correlated with the first ionisation potential of this compound[159,285,293–295]. Here however, it must be borne in mind that such a correlation is well achieved in a series of monotypical compounds, for example, in a series of ketones or esters[296–299].

From this point of view, taking into account that the bonding of the valence electrons of the sulphur atom is weaker than that for the oxygen atom, a higher electron-donating ability is to be expected for the sulphur-containing compounds. For typical donor–acceptor complexes with charge transfer the ability for complex formation is usually, with certain exceptions[300], higher for sulphur-containing compounds[145,163,301–304]. However, such a relation is not observed between the electron-donating ability of SR_2 and OR_2 and the strength of the HB formed by them with the same RX–H.

The experimentally observable higher ability of oxygen-containing compounds to form HB compared with that of their sulphur-containing analogues must be regarded from the viewpoint of the difference in the electronic structure of the sulphur and oxygen atoms.

Schneider[290] explains the difference in the proton-withdrawing abilities of sulphur and oxygen in the formation of HB by the degree of *s*-character of the orbitals of their non-generalised electrons. The unshared pairs of electrons of the sulphur and oxygen occupy hybrid *sp*-orbitals. According to published data the strength of the HB depends on the magnitude of the *s*-character of the hybrid *sp*-orbitals of the lone pair. For example, ethers (sp^3 hybridisation, 25% *s*-character) form stronger HB than ketones (sp^2 hybridisation, 33% *s*-character).[159,305] However, the strength of the HB formed by the lone pair increases with decrease in the *s*-character of its orbitals only up to a certain limit. For example, ethylene oxide, the lone pairs of which occupy pure *s*- and *p*-orbitals (hybridisation is absent) form less stable HB than ethers[159].

Hence the strength of the HB depends on the magnitude of the atomic dipole and the degree of spatial localisation of the lone pair: an increase in the *s*-character in the *sp*-hybrid orbital leads to a decrease in the asymmetry of the cloud of the unshared pair relative to the nucleus and to its spreading in space, which reduces the energy of interaction with the hydrogen atom. In ethers (esters) (Table 10) the C–O–C valence angle is close to 109°, but in the corresponding thioethers the C–S–C angle is always 7–12° less[306], that is, the orbitals of the lone pairs in the thioethers exhibit a considerably greater *s*-character than in ethers, in consequence of which the thioethers form less stable HB[159,160]. In triethyl phosphate the oxygen has sp^2 hybridisation and in triethyl phosphorothioate the unshared pairs of the sulphur occupy almost pure *s*- and *p*-orbitals (this also occurs in the C=O group as compared with the C=S group), which also leads to the P=S⋯H–O (C=S⋯H–O) HB being weaker than the P=O⋯H–O (C=O⋯H–O) HB.

Ginzburg[159] considers that the low energy of formation of HB involving a sulphur atom as the proton acceptor may also be partly due to the greater *s*-character of the lone pair orbitals. He thinks the main reason is that on going from an oxygen atom to a sulphur atom there is an increase in the principal quantum number of the electrons of the outer clouds which is accompanied by an increase in the symmetry of the lone pair orbitals and a decrease in their spatial localisation. For example, sulphur is known to form less stable covalent bonds than oxygen with the same atom. Consequently, the degree of overlap of the electron clouds in a C–S bond is less than in the C–O bond, that is, there is weakening of the bond owing to the orbitals of the sulphur atom being less localised in space. The greater "spreadability" of the orbitals of the sulphur atom with lone pairs than the corresponding orbitals of the oxygen atom is also mainly responsible for the lower ability of the sulphur atom to form HB in sulphur-containing compounds in comparison with the oxygen atom in their oxygen-containing analogues.

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Institute of Inorganic Chemistry,
Latvian SSR, Riga

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The Acid Properties of the Amino-group

A.F.Pozharskii and E.A.Zvezdina

The acid properties of primary *C*-amino-groups in amines, amides, and amidines have been examined. The methods of preparation and the physical and chemical properties of the metal salts of amines are discussed.
The bibliography includes 219 references.

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I. INTRODUCTION

Amino-compounds are usually regarded as bases capable of combining with a proton to form an ammonium ion (I). A less well known property of the NH_2 group is its capacity for acid dissociation. Indeed primary amines can be regarded as dibasic acids, which, following the ionisation of N–H bonds, can give rise to two series of conjugate bases—the monoanion (II) and the dianion (III):

$$\underset{(I)}{\overset{+}{R}NH_3} \overset{H^+}{\rightleftarrows} \underset{(II)}{RNH_2} \rightleftarrows \underset{(III)}{RNH^-} + H^+ \rightleftarrows RN^{2-} + 2H^+ .$$

Many investigations of methods for the preparation of *N*-anions of type (II) and (III) and their chemistry have been made, but there are almost no reviews on the acid properties of the amino-group. In the literature there exists only a brief compilation of data of metal salts of amines in a handbook[1], a review of magnesylamines[2], and a monograph[3] in which the ionisation of N–H bonds in liquid ammonia is considered. Strange as it may seem, the question of the acid properties of the amino-group is not discussed either in the extensive monograph[4] published in 1968 and specially devoted to the chemistry of the amino-group.

The main aim of the present paper is to review the accumulated literature data concerning the acid properties of the primary amino-group linked to a carbon atom. The review is thus devoted to aliphatic, aromatic, and heterocyclic amines and also to acid amides and amidines. Compounds in which the amino-group is linked to non-carbon atoms (hydrazines, halogenoamines, etc.) are not considered. Selected data on the acid properties of secondary amines are discussed.

The first section of the review is concerned with the acidity of the N–H bonds in various amino-compounds and with methods for the preparation of *N*-anions. The second section deals with the chemical properties of *N*-anions and their employment in organic synthesis. By analogy with carbanions[5], *N*-anions can be defined as conjugate bases of the corresponding N–H acids. The term "*N*-anions" thus refers to all salts of primary amines with alkali metals. It is then immaterial whether the M^+ ion is linked to the *N* anion with formation of a closely linked ion pair or whether the N–M bond is fully ionised. Only in those cases where the N–M bond is clearly covalent (>N–HgR, magnesylamines) is the employment of the term "*N*-anion" unjustified.

II. METHODS OF PREPARATION OF *N*-ANIONS

1. IONISATION OF N–H BONDS

a. General Information about the Acidity of the Amino-group. Solvents and Bases Inducing the Ionisation of N–H Bonds

The acidity of N–H bonds is usually much lower than that of O–H bonds. For example, ammonia, the simplest N–H acid, is weaker by 20 powers of 10 than water [pK_a = 34 (Smith[3])† and 14 respectively]. Therefore N–H bonds in amines are as a rule ionised in non-aqueous solvents by treatment with strong bases. The solvents employed are aromatic hydrocarbons and ethers: tetrahydrofuran (THF), dimethoxyethane, dioxan, etc., dimethyl sulphoxide (DMSO), and hexamethylphosphoramide (hexametapol or HMPA). Liquid ammonia is particularly valuable as a solvent, because it exhibits a high solvent and ionising power.

The bases most often used to ionise N–H bonds are alkali metal amides and organometallic compounds. Sodium hydride and alkali metals are frequently employed for this purpose. Alkali metal and ammonium hydroxides can also be used to ionise relatively strong N–H acids. However, when the pK_a of the amine is appreciably above 14–16, it is necessary to use a solvent or system of solvents in which hydroxide ions have an enhanced reactivity. The DMSO–water system has been used to ionise amines with pK_a values not exceeding 25–26.[8] Thus in an aqueous mixture containing 99.6 mole % DMSO, it was possible to ionise 3-chloroaniline (pK_a = 25.6) by treatment with tetramethylammonium hydroxide[9]. Overall, the bases enumerated can be arranged in the following series in terms of their ionising activity: carbanions (alkyl- and aryl-metals), sodium hydrides, alkali metal amides, alkali metals, and alkali metal hydroxides.

In order to follow the acid–base reaction and to determine the number of ionising N–H bonds when amines in aprotic solvents are treated with lithium alkyls, metal amides, and metal hydrides (or the metals themselves), the gases evolved (hydrocarbon, ammonia, and hydrogen respectively) are measured quantitatively. When alkali

† Other values for the ammonia pK_a are also quoted in the literature: 35 (Bell[6]) and 36 (Audrieth and Kleinberg[7]). They all refer to 33°C.

metal amides are employed in liquid ammonia, it is difficult to determine which type of species (the monoanion or the dianion) is formed as a result of the reaction. In this case one relies on chemical evidence, physical methods, or the elemental analysis of the salt isolated. It is very convenient to follow the ionisation of N–H acids in liquid ammonia when the acids are treated with alkali metals [10]. The process is carried out by the gradual addition of sodium (or potassium) to a solution (or suspension) of the amine in liquid ammonia. Apart from the evolution of hydrogen, the occurrence of the reaction is demonstrated by rapid (1–2 min) disappearance of the initial blue colour characteristic of solutions of alkali metals in liquid ammonia. The number of ionised N–H bonds is inferred from the amount of metal required to form a stable blue colour.

It is noteworthy that certain amines (for example 1-alkyl-5-aminobenzimidazoles and aniline) do not react with sodium in liquid ammonia. Nevertheless their anions, obtained by another procedure, are capable of existing in this solvent without appreciable ammonolysis‡. There is a fairly small number of quantitative data on the acidity of primary amines. On McEwen's thermodynamic scale [11] (in ether), the same $pK_a = 27$ is quoted for three aromatic amines: aniline, *p*-toluidine, and *p*-anisidine. Although the acidity of aniline specified by the pK_a is probably close to the true value, it is unlikely that the *p*-methyl and *p*-methoxy-groups have no appreciable influence on the acidity of the NH_2 group (by analogy with the influence of these groups on the acidity of the amino-nitrogen).

Systematic determinations of the acid dissociation constants of series of anilines and diphenylamines containing electron-accepting substituents have been made by Stewart and coworkers [8,9,12,13]. They employed a technique in which H_- functions§ were derived for various indicators and solvent systems. Using the pyridine–water, sulpholane–water, and DMSO–water solvent systems and tetramethyl- and trimethylbenzylammonium hydroxides as bases, they determined spectrophotometrically the acid dissociation constants of amines up to $pK_a = 25.6$.

For the determination of the acidity of relatively strong N–H acids ($pK_a < 19$), other solvent systems were also proposed: ethylenediamine–water [14], ethanolamine–water [15,16], hydrazine–water [18,19], t-pentyl alcohol–water [20], and ethanol–water [21]. It is remarkable that the pK_a of the same N–H acids, determined in different solvents of the above series, differ little from one another with rare exceptions.

The use of liquid ammonia as a solvent made it possible to extend the measurements to the region of even lower acidities of amines. Three groups of investigators have worked on the development of an acidity scale for arylamines in liquid ammonia [22–24]. With the aid of ^{1}H NMR, Birchall and Jolly investigated the position of acid–base equilibrium in a mixture of two acids HA and HB in liquid ammonia in the presence of sodamide [22]. On the basis of the results, the difference between the strengths of the two acids was determined from the following formula:

$$\Delta pK_a = \lg\left[\frac{(HB)}{(B^-)}\right] - \lg\left[\frac{(HA)}{(A^-)}\right] .$$

The authors then found the difference $\Delta pK'_a$ between the acidities of the next acid pair (HB and HC). Having accumulated a large number of such measurements, they constructed a relative acidity scale for aromatic amines in liquid ammonia, in which 2,5-dichloroaniline, the most acidic of the amines investigated, was adopted as a standard ($pK_a = 0$). This scale covers a range of 6.58 pK_a units towards lower acidities. A disadvantage of liquid ammonia proved to be the impossibility of measuring the acidities of stronger N–H acids, in particular nitroanilines, since the latter formed Meisenheimer type complexes with ammonia or the amide ion.

Takemoto and Lagowski, who employed ^{1}H NMR combined with spectrophotometric analysis¶ of the position of equilibrium, related the acidities of many weak N–H and C–H acids and thereby established an absolute acidity scale in liquid ammonia [23]. *NN*-Dimethyl-*p*-phenylenediamine (the weakest of the N–H acids, whose pK_a has been determined) and di-(*p*-tolyl)methane were selected as the linking pair of N–H and C–H acids. The acidity scale of Takemoto and Lagowski [23] covers the range of 13 pK_a units, the limit of the series corresponding to 2,5-dichloroaniline.

Herlem and Thiebault calculated the acid dissociation constants of substituted anilines from the results of their potentiometric titration in liquid ammonia with a potassamide solution using a hydrogen electrode [24]. It is noteworthy that the pK_a (Table 2) determined by the ^{1}H NMR and potentiometric methods differ from one another by 7–12 powers of 10 in absolute magnitude. It is at present difficult to say whether this is a consequence solely of differences in the temperatures at which the measurements were made (+25 °C for the ^{1}H NMR method and −60 °C for the potentiometric method) or whether some other factors also play a role. At any rate the acidities of liquid ammonia at +25° and −60 °C [$pK_a = 27.7$ (Coutler et al. [25]) and 32.5 (Herlem [26]) respectively] do not differ from one another very markedly.

b. Alkylamines and Cycloalkylamines

Alkylamines are even less acid compared with ammonia (there are no quantitative data). Therefore they cannot be converted into salts in liquid ammonia either with the aid of alkali metal amides [27] or the metals themselves [7]. However, in aprotic inert solvents (toluene, octane, etc.) or altogether in the absence of a solvent, alkylamines and

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‡ The term "ammonolysis" implies an acid–base reaction between ammonia and the conjugate states of an acid BH weaker than ammonia:

$$B^- + NH_3 \rightleftarrows BH + NH_2^- .$$

The weaker the BH acid the greater the shift of the above equilibrium to the right.

§ The function H_- defines the capacity of the solvent to abstract a proton from a neutral acid HA and is calculated from the formula [12]

$$H_- = -\lg\frac{a_{H^+}f_{A^-}}{f_{HA}} = pK_a + \lg\frac{[A^-]}{[HA]} .$$

In dilute aqueous solutions H_- is identical with pH.

¶ One of the disadvantages of the spectrophotometric method for solutions of liquid ammonia is the impossibility of measuring the acidity of amines weaker than aniline. This is due to the insignificant degree of ionisation of such acids and the consequent masking effect of the amide present in large excess, which absorbs at 350 nm. [22]

cycloalkylamines can be converted into metal salts by prolonged heating with alkali metal amides in nitrogen [28-30]. A necessary condition for the success of this reaction is the removal of the ammonia formed from the reaction zone. If ammonia is not removed, an equilibrium is established between the initial and final products [31]:

$$CH_3NH_2 + LiNH_2 \rightleftarrows CH_3NHLi + NH_3 .$$

Therefore it is technically simplest to obtain with the aid of this method metal salts of high-boiling amines (butylamines, cyclohexylamine, etc.).

Alkali metals dissolve in the lowest alkylamines to form blue solutions, the properties and structures of which are close to those of solutions of alkali metals in liquid ammonia [32]. However, on heating, a slow reaction takes place between alkylamines and cycloalkylamines on the one hand and the alkali metals on the other, and is accompanied by the evolution of hydrogen and the formation of the corresponding salt. This reaction is frequently employed for preparative purposes and is usually carried out without a solvent:

$$RNH_2 + M \rightarrow RNH^-M^+ + {}^1/_2H_2 .$$

In the preparation of metal salts of methylamine by this method, one should guard against a side reaction involving the formation of cyanides [33,34]. The conversion of methylamine into potassium methylamide can be achieved smoothly with the aid of potassium hydride [34].

The best method for the preparation of lithium salts of alkylamines and cycloalkylamines is apparently the reaction of amines with organolithium compounds. Usually lithium alkyls in benzene, hexane, or ethers are employed for this purpose. Table 1 gives a compilation of certain data for the preparation of metal salts of alkylamines and cycloalkylamines.

Table 1. Metal salts of certain alkyl- and cycloalkylamines.

Salt	Ionising agent	Conditions	Ссылки на литературу
CH_3NHLi	Li	60°, in sealed tube	33
CH_3NHK	KH	20-25°, 4-6 h	34
C_6H_5NHNa	—	—	29, 30
C_6H_5NHK	K	Ethylamine passed slowly over heated potassium	35
iso-C_3H_7NHNa	$NaNH_2$	Toluene, 121 h	29, 30
n-C_4H_9NHNa	$NaNH_2$	Toluene, 97-109°, 63 h	29, 30
t-C_4H_9NHLi	CH_3Li	Ether, 0°	36
n-$C_8H_{17}NHNa$	$NaNH_2$	—	29, 30
$C_6H_{11}NHLi$	n-C_4H_9Li	In excess of cyclohexylamine	37
$C_6H_{11}NHNa$	$NaNH_2$	Heating in iso-octane	—
$C_6H_{11}NHCs$	Cs	In excess of cyclohexylamine	37

c. Arylalkylamines

On going from methylamine to benzylamine, diphenylmethylamine, and finally to triphenylmethylamine, the acidity of N–H bonds should increase somewhat owing to the electron-accepting influence of the aryl group. Simultaneously there should be an even greater increase in the acidity of the C–H bonds adjoining the amino-group. As a result, when strong bases act on benzylamine and particularly on diphenylmethylamine, the N–H and C–H bond ionisation processes compete. Hauser et al. established that, when diphenylmethylamine is treated with potassamide in liquid ammonia, a mixture of the carbanion (IV) and the *N*-anion (V) is formed[39]:

$$(C_6H_5)_2CH{-}NH^- \underset{NH_3}{\overset{KNH_2}{\rightleftarrows}} (C_6H_5)_2CH{-}NH_2 \overset{KNH_2}{\underset{NH_3}{\rightarrow}} (C_6H_5)_2\bar{C}{-}NH_2$$
(V) (IV)

$\downarrow$ 1. CO_2 2. H^+ $\downarrow$ 1. CO_2 2. H^+

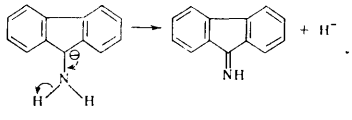
$(C_6H_5)_2CHNHCOOH$ $(C_6H_5)_2C(NH_2)COOH$

(VII) (VI)

The formation of the carbanion (IV) is proved by the appearance of the red colour characteristic of arylalkyl carbanions and also its conversion into the aminoacid (VI) when the reaction mixture is carboxylated after the evaporation of ammonia. The presence in the mixture of the *N*-anion (V) has been less definitely established. The presence of the carbamic acid (VII) in the carboxylation products cannot serve in this case as unambiguous proof that the *N*-anion is present, since the initial diphenylmethylamine also gives rise to the acid (VII) on interaction with CO_2.

The formation of the carbanion is promoted by its resonance stabilisation, while the *N*-anion is stabilised in arylalkylamines only by the *-I* effect of the arylalkyl group.

Benzylamine itself is probably still a very weak acid. Thus Picon failed to obtain sodium benzylamide by the reaction of benzylamine with sodium or with $NaNH_2$ in liquid ammonia even after a long time in an autoclave [38]. However, the appearance of a red colour when benzylamine is treated with various bases [39-41] indicates the formation of a certain amount of carbanions. This is also suggested by certain indirect data. For example, 9-aminofluorene, diphenylmethylamine, and benzylamine are converted into the corresponding imines on standing in liquid ammonia in the presence of potassamide [42]. It appears likely that the reason for this phenomenon consists in the β-elimination of a hydride ion from the corresponding carbanion:



The fact that the amino-group in arylalkylamines is more acid in ammonia than in alkylamines can be inferred from the existence in liquid ammonia, without appreciable ammonolysis, of the dipotassium salts of diaminodiphenylmethane (VIII), obtained by the addition of two KNH_2 molecules to benzophenoneimine [43]:

$$(C_6H_5)_2C{=}NH + 2KNH_2 \rightarrow (C_6H_5)_2C(NHK)(NHK)$$

(VIII)

In this connection, it is difficult to understand why triphenylmethylamine fails to give an *N*-anion when acted upon both by potassamide in liquid ammonia [44] and by alkali metals in liquid ammonia or in ether [45]. Sodium and potassium in liquid ammonia cleave the C–N bond in triphenylmethylamine with formation of a carbanion and an amide ion [44]:

$$(C_6H_5)_3C{-}NH_2 \xrightarrow{M} \begin{cases} (C_6H_5)_3NH^-M^+ \\ (C_6H_5)_3C^-M^+ + MNH_2 \end{cases}$$

Steric factors can hardly be responsible for the difficulty of the ionisation of the N–H bonds in triphenylmethylamine, since triphenylmethane, where the steric effect

should be even more pronounced, readily ionises in liquid ammonia in the presence of metal amides and alkali metals. Such behaviour of triphenylmethylamine suggests that the ionisation of diphenylmethylamine and benzylamine (weaker N–H acids than triphenylmethylamine) involves preferentially the C–H bonds, i.e. the formation of a carbanion. Metallation of CH–NH systems is fairly common in organic chemistry. For example, acetamido-[46-48] and benzamido-malonic esters[49] give rise to carbanions and not *N*-anions when acted upon by bases, a fact which is used in the synthesis of aminoacids.

d. Arylamines

Although aromatic amines are very weak N–H acids, their acidity is nevertheless much greater than that of aliphatic amines and ammonia. This can be accounted for by the possibility of the resonance stabilisation of the arylamine *N*-anions:

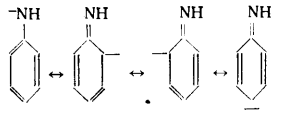
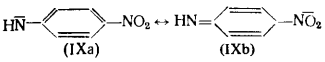


Table 2. Acid dissociation constants (pK_a) of a series of anilines.[a]

Substituent in benzene ring of aniline	Solvent, temp., °C			Substituent in benzene ring of aniline	Solvent, temp., °C		
	+25[9,12,13][b]	NH_3, +25[23]	NH_3, −60[24]		+25[9,12,13][b]	NH_3, +25[23]	NH_3, −60[24]
H	27.3[c]	21.2	28.8	4-Cl	—	19.9	27.4
2-NO_2	17.88	—	—	4-CN	22.68	15.9	28.5
3-Cl	25.63	—	—	4-NO_2	18.37	—	—
3-CF_3	25.40	18.7	—	2,4-$(NO_2)_2$	15.00	—	—
4-CH_3	—	22.1	—	2,4,6-$(NO_2)_3$	12.20	—	—
4-$N(CH_3)_2$	—	25.6	—				

[a] The acidity constants of many other anilines are quoted in the literature[9,12,13,23,24].
[b] The average pK_a values for various solvent systems: DMSO–water (99.9 mole % DMSO), sulpholane–water (95.5 mole % sulpholane), and others.
[c] pK_a = 27.3 was obtained for aniline by extrapolation.

Table 2 shows that aniline is a stronger acid by 6–7 powers of ten than ammonia. Introduction of electron-accepting substituents into the benzene ring of aniline cause an even greater increase of the acidity of the NH_2 group and the 2,4,6-trinitroaniline anion can exist even in water. The inductive effect of the nitro-group in the series of anilines is greater than in the series of phenols. It is believed that in the *N*-anions of *o*- and *p*-nitroarylamines most of the negative charge is localised at the NO_2 group, i.e. structure (IXb) makes a large contribution to the resonance state[50]:



In certain cases (3-nitroaniline), on treatment with hydroxyl-containing bases the ionisation of the N–H bond is accompanied by a competing process involving the nucleophilic addition of the $O\bar{H}$ ion to the aromatic ring. The two reactions can be distinguished spectrophotometrically: in contrast to the addition process, ionisation takes place instantaneously[9].

It has been found[22] that there is a satisfactory correlation between the σ constants of substituents (σ^- constants must be employed for the *p*-NO_2, *p*-CN, and *p*-F substituents) and the pK_a values of substituted anilines with a constant $\rho = -5.3$. Such a high value of ρ shows that the acidity of aniline depends significantly on the effect of substituents and, as shown by experiment, to a greater extent than the acidity of anilinium ions. The ρ constant for the acid dissociation of substituted diphenylamines is also very high (−4.07).[9]

Stewart and Dolman[50] (see also Birchall and Jolly[22]) established that there is a fairly satisfactory linear relation between the basicities pK_{BH^+} (acidities of anilinium ions) and the acidities of pK_{HA} of substituted anilines and diphenylamines (with the exception, for reasons stated above, of compounds with nitro-groups):

$$pK_{HA} = 21.4 + 1.30\ pK_{BH^+} . \quad (1)$$

This equation can be used for an approximate estimation of the acidities of amines whose pK_{HA} have not been determined for one reason or another, but the basicity pK_{BH^+}, which can be determined more readily and accurately, is known. For example the basicities of aniline, *p*-toluidine, and *p*-anisidine are 4.60, 5.10, and 5.34,[51] from which we have the acidities 27.52, 28.03, and 28.34 respectively. The value 27.5 for aniline agrees satisfactorily with other data[11,24].

For preparative purposes, when it is necessary to employ aprotic solvents, the *N*-anions of aromatic amines are obtained by treating the amines with sodium hydride[52], lithium alkyls[53], lithium aryls[54], or organomagnesium compounds[2,55-57]. In the cold, the metal usually substitutes one hydrogen atom in the NH_2 group, while on brief heating the second hydrogen atom is also readily replaced at a temperature as low as 35–40°C:

$$ArNH_2 + RMgX \xrightarrow[-RH]{20-25^\circ} ArNHMgX \xrightarrow[\Delta]{RMgX} ArN\begin{matrix}MgX\\MgX\end{matrix} + RH .$$

This reaction serves as a basis for the quantitative determination of active hydrogen in arylamines[58].

At room temperature, neither sodium nor sodamide reacts with aniline at an appreciable rate, but, when aniline is refluxed with these bases in xylene[59] or in the absence of a solvent[35,60], the sodium salt of aniline is formed fairly readily. The use of HMPA, the high ionising power of which makes it possible to carry out the process under mild conditions[61,62], is extremely convenient in the preparation of sodium arylamides. It is believed[61] that, when two equivalents of sodamide are employed in HMPA, the disodium salts of aromatic amines are also formed. However, this conclusion is based on alkylation data which, as will be shown below, do not constitute convincing proof.

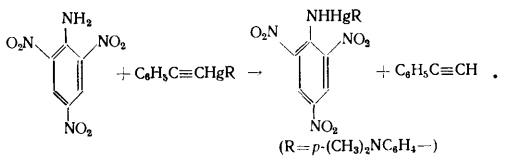
The preparation of the anions of more acid amines (for example *p*-nitroaniline) can be achieved in DMSO by treatment with alkali metal hydroxides[9].

The generation of the *N*-anions of aromatic amines in liquid ammonia requires special consideration. The ionisation of the N–H bonds in aniline and its derivatives with electron-donating substituents on treatment with alkali metals or $NaNH_2$ takes place in this solvent only at room

temperature and under pressure [38]. Under the usual conditions for experiments in liquid ammonia (temperature between −33° and −60°C), the N−H bonds in aniline cannot be ionised by treatment with alkali metals or $NaNH_2$. This is very surprising bearing in mind that the sodium and potassium salts of diphenyl- and triphenylmethane, which are weaker C−H acids than aniline, are readily formed in liquid ammonia under analogous conditions. Probably the solvating power of liquid ammonia in relation to carbanions is greater than in relation to *N*-anions.

According to the data of Bunnett and Moyer [63], when aniline is treated with potassamide in liquid ammonia at a temperature as low as at −33°C, potassium anilide is readily formed. The ease of this reaction can probably be explained by the higher solubility of potassamide in liquid ammonia (450 g litre^{-1} at −33°C) compared with sodamide (1.5 g litre^{-1} 25°C). [64] However, one should note that rigorous proof of the complete conversion of aniline into its *N*-anion was not obtained, since the salt was not isolated in a pure form.

In a series of investigations, Nesmeyanov and Kravtsov showed that aromatic amines containing also acidifying substituents such as NO, NO_2, and −N=N− readily form arylmercury derivatives on reaction with arylmercury hydroxides [65-68]. For fairly acid amines (picramide), arylmercury derivatives of acetic acid, phenylacetylene, or *p*-nitroaniline can also be employed as bases [65]:



Aniline itself and its *p*-chloro- and *p*-bromo-derivatives do not form arylmercury derivatives under these conditions [65].

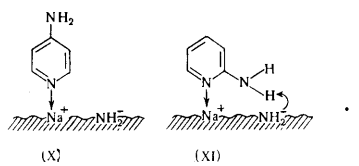
e. Heterocyclic Amines

In the amino-derivatives of aromatic aza-systems, the amino-group is much more acidic than aniline owing to activating effect of aza-nitrogen. It appears that there are no quantitative literature data for the acidities of *N*-heteroaromatic amines. However, one can suppose that the pK_a for 2- and 4-aminopyridines should be intermediate between the acidities of 2-nitroaniline (pK_a = 17.9) and 2,4-dinitroaniline (pK_a = 15.0). This estimate is based on a comparison of the values of σ_p for the pyridine nitrogen atom and the NO_2 group, which are +0.93 and +0.778 respectively [69] (the literature values of σ_o for the pyridine N atom are +0.81, +1.02, etc.). [69]

It is therefore not surprising that α-amino-derivatives of pyridine [59,70-79], quinoline [88], isoquinoline [71], thiazole [80], benzimidazole [71], and pyrimidine [70,78,81] readily form salts when acted upon by alkali metal amides and hydrides, alkali metals themselves, and even their hydroxides under certain conditions [79]. Aromatic hydrocarbons, liquid ammonia, HMPA, and sometimes ether or dioxan are usually employed as solvents. It is noteworthy that in only a few cases these salts were isolated in a crystalline state and investigated [59,70,74]. Usually, after preparation in solution (liquid ammonia, HMPA) or in a suspension (ether, dioxan, hydrocarbons), the salts were immediately introduced into further reactions without preliminary isolation.

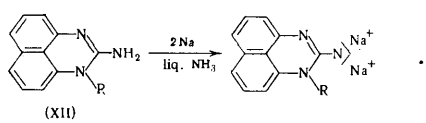
In β- and γ-aminoheterocycles containing a pyridine *N*-heteroatom, the amino-group is also appreciably activated and readily ionises when treated with alkali metals or their amides in liquid ammonia or in HMPA. [71,82,83] However, the formation of metal salts of such amines in weakly polar aprotic solvents proceeds with greater difficulty. For example, 4-aminopyridine hardly reacts (in contrast to 2-aminopyridine) with sodamide in ether [84], while in benzene and xylene the reaction proceeds very slowly even at 140−150°C and can hardly be used for preparative purposes [59,84].

This observation is in sharp contrast to the known sequence of acidities of the CH_3 group in isomeric picolines: 4-CH_3 > 2-CH_3 > 3-CH_3. [85] One of the possible reasons for the difficulty of the ionisation of the NH_2 group in non-polar aprotic solvents is that the reaction takes place in a heterogeneous medium. Therefore the amino-derivative may be sorbed on the surface of sodamide crystals via the coordination of the pyridine N-atom (the most basic centre in the molecules of α- and γ-aminoheterocycles) to the Na^+ ion as in (X). It is quite clear that, for geometrical reasons, such sorption should greatly increase the ionisation of the NH_2 group in 4-amino-derivatives. On the other hand, in the case of α-amino-compounds it should serve as an additional factor promoting the ionisation of the N−H bond, as in (XI):

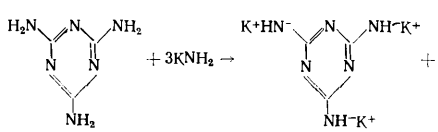


In solvents where alkali metal amides are soluble (liquid ammonia, HMP), the ionisation of N−H bonds takes place equally readily for both α- and γ-amino-derivatives owing to the homogeneity of the system.

In *N*-heteroaromatic amines, one may expect a greater ease of formation of dianions compared with aromatic amines. Nevertheless, the vast majority of amines, including all three pyridylamines, form monoanions in liquid ammonia when acted upon by alkali metals and apparently metal amides [71]. Among all the amines investigated in this respect, only the 2-amino-derivatives of perimidine (XII) and aceperimidine form dianions under these conditions [71]:



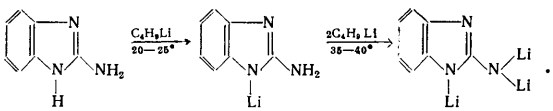
Triamino-1,3,5-triazine (melamine) exhibits very acidic properties. In liquid ammonia it can give rise to mono-, di-, and even tri-anions when acted upon by potassamide [86]:



The amino-group in a benzene ring condensed with a heterocyclic nucleus can be both actived and passivated, depending on the nature of the latter. For example, aminoquinolines in liquid ammonia readily form anions on treatment with potassamide [87]. On the other hand, 1-R-5-aminobenzimidazoles cannot be converted into

N-anions in liquid ammonia by treatment with alkali metals or their amides [71]. Reductive cleavage of azides, discussed in section II, 2, gives very satisfactory results in the synthesis of such *N*-anions.

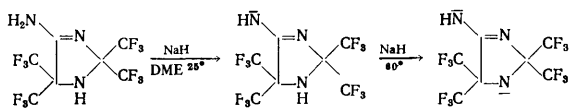
In *N*-heteroaromatic amines containing an endocyclic N–H pyrrole bond in addition to the NH_2 group, the former is as a rule more acidic and ionises first. This applies also to compounds containing an amino-group in the side chain (histidine [88], tryptophan [89]) and to true heteroaromatic amines. Thus, when 2-aminobenzimidazole (XIII) is treated with butyl-lithium or with butylmagnesium bromide, initially the H atom of the endocyclic N–H bond is substituted and only then, on heating to 40°C, is the trilithium salt or trimagnesylamine formed [90]:



(XIII)

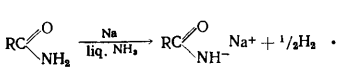
When the amine (XIII) is treated with an excess of an alkali metal amide in liquid ammonia, an equilibrium mixture of di- and tri-anions is formed, with the former predominating [91]. When sodium or potassium is employed as the base, the reaction stops at the monoanion stage [91].

In amino-derivatives of certain partly hydrogenated *N*-heterocycles, the amino-group may be ionised first provided that it is conjugated with an endocyclic C=N bond [92]:



f. Carboxylic Acid Amides

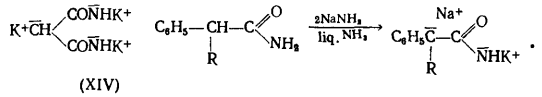
The amides of carboxylic and particularly thiocarboxylic acids exhibit a much greater acidity than other amino-compounds (Table 3). Thus the pK_a's for acetamide and benzamide are in the range 14–15. [93,94] The acidity of thioacetamide in liquid ammonia at −60°C is estimated as 4.6 pK_a units [24]. When treated with alkali metals or their amides, acid amides in liquid ammonia readily form monoanions [95–98]:



The report that dianions are formed under these conditions [96] was subsequently disproved by the same author [64]. Nevertheless, bearing in mind the very high acidity (among N–H acids) of acid amides, the possibility of the existence in liquid ammonia of their dianions, generated by another procedure, appears to be extremely probable.

Franklin obtained in liquid ammonia and isolated in a crystalline form a large series of carboxylic acid amide salts with alkali and alkaline earth metals [64]. When acid amides are treated with phenylmercury hydroxide, one H-atom of the NH_2 group also ionises and a phenylmercury derivative is formed [65].

The amides of dibasic acids can form in liquid ammonia also polyanions, in which, however, each amino-group carries only one negative charge. For example, malonamide forms a trianion (XIV) when treated with potassamide in liquid ammonia [64]. Phenyl- and diphenyl-acetamides give rise to *CN*-dianions under analogous conditions, the N–H bond being the first to ionise [99,100]:



(XIV)

The use of organometallic reagents gives rise to a wide scope for the ionisation of N–H bonds in acid amides. Hauser and coworkers showed that, when aliphatic and aromatic acid amides are treated with an excess of butyl-lithium in THF or ether, dilithium salts are formed, to which the structure of *ON*-dianions was ascribed [101,102]:

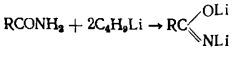
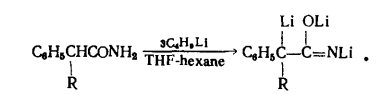


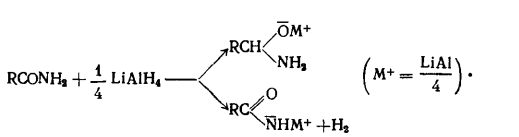
Table 3. Acid dissociation constants (pK'_a) of certain N–H acids.

Compound	pK'_a	Conditions	Refs.	Compound	pK'_a	Conditions	Refs.
Acetamide	14	NH_3	3	Thiourea	8.5	NH_3,—60°	24
"	15	25°	93, 94	*N*-Phenylthiourea	3.8	NH_3,—60°	24
Benzamide	14—15	—	93, 94	Semicarbazide	25—33	NH_3,—33°	112
Thioacetamide	4.6	NH_3,—60°	24	Carbohydrazide	21—25	NH_3,—33°	112
Urea	12.9	NH_3,—60°	24	*NN'*-Diphenylguanidine	10.7	NH_3,—60°	24
"	25—33	NH_3,—33°	112	Cyanamide	7	NH_3	3
NN'-Diphenyl urea	7.0	NH_3,—60°	24	Hydrazine	13.5	NH_3,—60°	24

The reaction with organomagnesium compounds takes place similarly, and is used in the quantitative determination of active hydrogen in acid amides by the Tserevitinov method [103]. The amides of aliphatic-aromatic acids, containing a C–H bond in the α-position relative to the $CONH_2$ group, form trianions when acted upon by an excess of butyl-lithium [100,101]:



When acid amides are treated with lithium aluminium hydride, two competing reactions take place: the addition of $LiAlH_4$ to the C=O group and the ionisation of the N–H bond [104]:



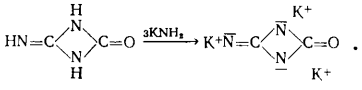
Usually the addition reaction takes place preferentially, but when R is a fairly bulky group, mono- or di-metallated derivatives are mainly produced.

g. Urea, Thiourea, and Guanidine

It was established that, when acted upon by alkali metal alkoxides in an alcoholic medium, urea behaves as a monobasic acid [105]. However, when sodium [106,107] or potassamide [96,108] are employed as bases in liquid ammonia, it

is possible to obtain both mono- and di-anions. In contrast to the monopotassium salt of urea, its dipotassium salt is sparingly soluble in liquid ammonia and is usually precipitated when a second equivalent of the base is added[109]. The monosodium salt is also sparingly soluble in liquid ammonia[106]. Therefore it is clear that, when urea is treated with two equivalents of sodium or sodamide, a mixture of mono- and di-sodium salts is formed, i.e. the second ionisation takes place with somewhat greater difficulty. The monosodium salt of urea has been isolated in a crystalline form and investigated in detail[106].

Among urea derivatives, cyanourea, the cyclic form of which gives rise to a trianion when treated with potassamide in liquid ammonia, is of interest[110]:



In water cyanourea behaves as a monobasic acid.

Thiourea and guanidine can also behave as mono- or di-basic acids depending on the conditions. The monosilver and dipotassium salts of guanidine[86] and the monopotassium[111] and dipotassium[109] salts of thiourea have been obtained. The formation of dipotassium salts of urea, thiourea, and guanidine in liquid ammonia has been demonstrated unambiguously[109] by the potentiometric titration of liquid ammonia solutions of these acids with a potassamide solution. On this basis, the following sequence of relative acidities has been established:

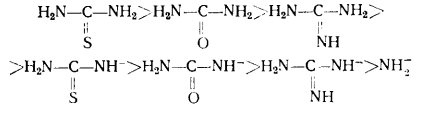
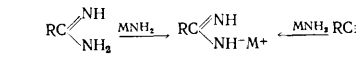


Table 3 presents quantitative data for the acidities of urea, thiourea, and certain related compounds. According to French workers, the first acid dissociation constants (pK'_a) of urea and thiourea in liquid ammonia are respectively 12.9 and 8.5.[24] The second dissociation constants (pK''_a) have not so far been determined, but, judging from the ease of formation of dianions by urea and thiourea in liquid ammonia, they should be in the range 25–30.

An attempt has been made to estimate the acidity of urea by titrating its ammonia solution with a solution of triphenylmethylsodium in the presence of indicators such as indene and fluorene[112]. It was found that the addition of even one drop of the triphenylmethylsodium solution to a mixture of urea and fluorene in liquid ammonia results in the appearance of the yellow colour characteristic of the fluorene anion. Assuming that pK_a for fluorene is 25, Corwin and Reinheimer[112] concluded that the acid dissociation constant of urea (judging from the experimental conditions, the constant is pK'_a) is in the range 25–33. However, this value contradicts all previously known facts concerning the acidity of urea and can probably be accounted for by the unsuitability of fluorene as an indicator in this case (possibly because of the greater kinetic acidity of fluorene, which is not always the same as the thermodynamic acidity).

h. Amidines

In water amidines behave as very powerful bases but in liquid ammonia they exhibit the properties of monobasic acids, readily forming monoanions when treated with alkali metals or metal amides[64,113]. A more usual method for the preparation of sodium and potassium salts of amidines involves the addition of an alkali metal amide to the corresponding nitrile[114,115]:

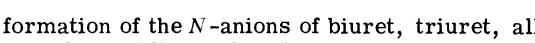


A large number of sodium, potassium, and calcium salts of aliphatic and aromatic amidines have been obtained in this way. The silver and copper salts of amidines, which are insoluble in liquid ammonia, can be obtained by the double decomposition between the potassium or sodium salt of the corresponding amidine and the metal nitrate[113].

i. Other Compounds

One of the simplest compounds containing the *C*-amino-group is cyanamide. It exhibits a very high acidity ($pK_a = 7$) and readily forms salts with alkali and alkaline earth metals in liquid ammonia. Numerous examples of such salts are quoted in a handbook[116] and in other publications[86,96].

Carbamic acid can exist in liquid ammonia in the form of the mono- and di-potassium salts, which are obtained by treating ammonium carbamate with potassamide[108]. When acted upon by potassamide in liquid ammonia, ethyl carbamate forms an unstable potassium salt which decomposes according to the following equation:[108]

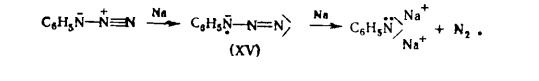


The formation of the *N*-anions of biuret, triuret, allophanic acid, biguanidine and certain other compounds with a *C*-amino-group in liquid ammonia has been discussed in a monograph[3].

2. REDUCTIVE CLEAVAGE OF N–X BONDS

a. Azides

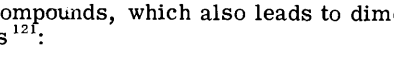
Phenyl azide is reduced by metallic sodium in boiling ether with formation of the disodium salt of aniline and evolution of nitrogen[117]. The reduction proceeds via the stage in which a radical-anion (XV) is formed; it was detected by its characteristic red colour and the ESR spectrum:



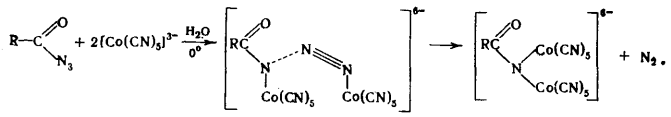
Later it was found for aromatic and heterocyclic azides that liquid ammonia is a very convenient solvent for this reaction[118,119]. The synthesis of *N*-anions via azides is the only one possible in those cases where the ionisation of the N–H bonds in the amino-group proceeds with difficulty or not at all[71].

Initially it was postulated that the dianions of aromatic amines obtained from azides are stable in liquid ammonia[118,119], although recently certain data have been obtained indicating their ammonolysis to the monoanions[71,120].

It was possible to reduce aromatic azides by organometallic compounds, which also leads to dimetal salts of the amines[121]:

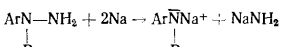


Only one example of reactions of this type is known for acyl azides [122]:

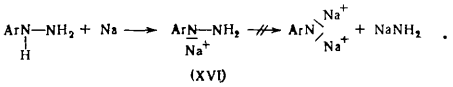


b. Hydrazines

In an unpublished study, referred to by Smith [3] and Watt [10], Fernelius and coworkers investigated the action of sodium in liquid ammonia on a large number of various substituted hydrazines. They established that, when the nitrogen atom linked to the benzene ring in aromatic hydrazines is not joined to a free hydrogen atom, the N–N bond undergoes reductive cleavage on treatment with sodium, which results in the formation of the sodium salt of a secondary amine:

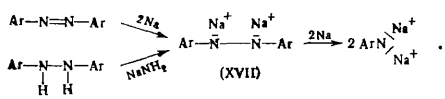


In hydrazines with a free N–H group in the α-position relative to the aromatic ring, the N–H α-bond is the first to ionise on treatment with sodium with formation of the resonance-stabilised N-anion (XVI), which is resistant to further reduction:



(XVI)

There are contradictory views in the literature concerning the possibility of the cleavage of the N–N bonds in the dianion of hydrazobenzene (XVII), formed when hydrazobenzene or azobenzene are treated with metal amides and alkali metals respectively:

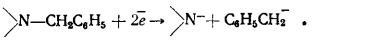


(XVII)

Data [123] supporting such cleavage, which leads to disodium anilide, were not subsequently confirmed [124]. According to the observations of the authors of the review, the N–N bond in the dianions of heterocyclic hydrazocompounds is not cleaved either, for example in 1,1′-dialkyl-2,2′-hydrazobenzimidazoles.

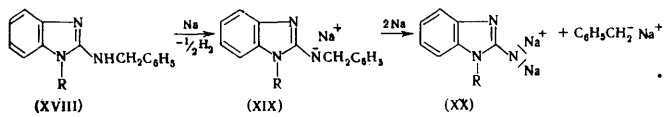
c. Cleavage of the N–C Bond in Benzylamines

The removal of the N-benzyl protecting group by solutions of alkali metals in liquid ammonia is a well known synthetic procedure. It is usually employed in the N-heteroaromatic series for compounds with a pyrrole nitrogen atom. The process takes place as a two-electron reduction of the C–N bond and leads to the formation of the N-anion of the secondary amine and the benzyl anion†, which subsequently undergoes ammonolysis and gives rise to toluene:



† The theory of reductive debenzylation with the aid of liquid ammonia solutions of alkali metals is described by Birch [125].

N-Benzyl derivatives of primary aromatic (for example benzylaniline [10]) and heteroaromatic amines enter into an analogous reaction. It has been shown for 2-benzylaminobenzimidazoles (XVIII) [90,120] that the action of sodium in liquid ammonia on such compounds begins with rapid ionisation of the N–H bond, which is followed by slow debenzylation of the N-anion (XIX). Ultimately, the amine dianion (XX) and the benzyl anion are formed and gradually undergo ammonolysis:



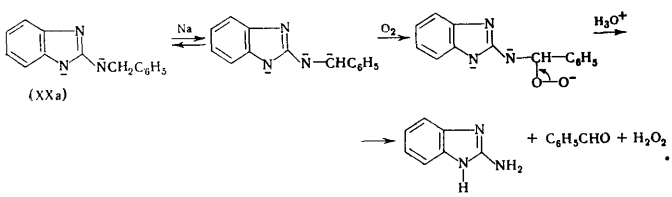
(XVIII) (XIX) (XX)

Reductive debenzylation proceeds more readily the greater the effective positive charge on the nitrogen atom to which the benzyl group is linked. Therefore the benzyl group joined to the pyrrole nitrogen atom is eliminated on treatment with sodium in liquid ammonia more readily than the benzyl substituent linked to an exocyclic amino-group [126,127].

If the benzyl group is joined to a negatively charged nitrogen atom, two outcomes are possible from the standpoint of the mechanism of the debenzylation process.

1. The negative charge on the nitrogen atom is effectively delocalised owing to conjugation with the aromatic π-electron system. In this case [a typical example is provided by the monoanion (XIX)] debenzylation still proceeds as a two-electron reductive process, albeit extremely slowly, and the reaction is accompanied by the formation of toluene.

2. The negative charge is located preferentially on the nitrogen atom. This case obtains when sodium acts upon 2-benzylaminobenzimidazole (XVIII, R = H) and on 1-benzyl-2-benzylaminobenzimidazole (XVIII, R = $C_6H_5CH_2$). [126] The dianion (XXa) is then formed initially. The addition of two-electrons to the C–N bond in this dianion should be extremely unfavourable on energy grounds. Indeed debenzylation should take place with difficulty and involve the formation of a considerable amount of benzaldehyde. Although the mechanism of this reaction is not in fact completely clear, it evidently includes an autoxidation stage and can be tentatively described by the following scheme:



(XXa)

Thus in principle one should distinguish two mechanisms of the debenzylation of benzylamines with the aid of solutions of metals in liquid ammonia—reductive and oxidative. The oxidative debenzylation mechanism requires further study.

Apart from the benzyl group, N-methoxymethyl [128] and other arylalkyl groups (ring-substituted benzyl groups, the diphenylmethyl group, the α-phenylethyl group [90], etc.) can undergo reductive elimination with formation of N-anions. When attempt was made to cleave the N–allyl bond by sodium in liquid ammonia, a difficulty was encountered owing to the reduction of the double bond of the allyl substituent, after which the N–C bond was no longer cleaved [129].

III. THE NATURE OF THE NITROGEN–METAL BOND AND THE STRUCTURE AND PHYSICAL PROPERTIES OF METAL SALTS OF AMINES

There have been few studies specially undertaken to investigate the nature of the nitrogen–metal bond in metal salts of amines. Two parameters of this bond, its polarity and the type of hybridisation of the N atom, can exert a major influence on the physical properties and reactivity of such salts. The use of Pauling's formula [130] $i = 100\,(1 - e^{-0.25(\chi_a - \chi_b)^2})$ to calculate the percentage ionic character of certain N–M bonds yields the results presented in Table 4 (here $\chi_N - \chi_M$ represents the difference between the relative electronegativites of nitrogen and metal atoms between which the bond is formed).

It follows from Table 4 that the bonds between nitrogen and alkali metals must be regarded as largely ionic, the amount of ionic character increasing in the sequence Li < Na < K. This agrees with the experimental measurements of the conductance of lithium [131] and caesium [132] cyclohexylamides in cyclohexylamine.

Table 4. Percentage of ionic character of certain nitrogen–metal bonds.

Bond	$\chi_N - \chi_M$	Amount of ionic character, %	Bond	$\chi_N - \chi_M$	Amount of ionic character, %
N—K	2.2	70	N—Mg	1.8	55
N—Na	2.1	67	N—Ag	1.2	30
N—Li	2.0	63	N—Hg^{II}	1.1	26

In magnesylamines, the N–Mg bond is equally covalent and ionic. The bond between nitrogen and metals such as copper, silver, and mercury is mainly covalent. Naturally, the degree of polarity of the N–M bond is also influenced by the type of hybridisation of the nitrogen atom and the nature of the hydrocarbon groups to which the nitrogen and metal atoms are linked (provided that the valence of the metal is greater than unity). These additional factors are not taken into account in the calculation of the percentage ionic character of the N–M bond.

Qualitative data on the amount of ionic character of the N–M bond agree fully with the properties of metal salts of amines. Thus silver and mercury salts of amines are as a rule resistant to the action of water and alcohol. They dissolve in certain organic solvents and can be actually recrystallised from them [68]. Although magnesylamines are usually readily decomposed by water, they are frequently soluble in ethereal solvents. In this respect they resemble the lithium salts of amines.

The sodium and potassium salts of alkylamines are highly hygroscopic and pyrophoric[34], like alkali metal amides. They are liable to explode in air and react vigorously with water and alcohols. Therefore they must be handled and stored in a completely inert atmosphere. Similar precautions must be observed in work with sodium, potassium, and lithium salts of arylamines and heterocyclic amines. However some of the latter (for example, the sodium salt of 2-aminopyrimidine [70,81]) are completely stable in air and are non-hygroscopic.

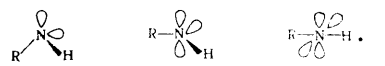
Many salts of amino-compounds with alkali metals are readily soluble in liquid ammonia, where they are apparently appreciably dissociated. This hypothesis is based on ultraviolet spectroscopic data for liquid ammonia solutions of potassamide [33], from which it follows that, depending on the concentration of the solution, the degree of dissociation of potassamide is 30–75%. DMSO [9,12,13] and HMPA [62] also exhibit a high solvent power in relation to metal salts of amines.

In solvents with a low dielectric constant, amides are dissociated into free ions only to an insignificant extent ($K_d \simeq 10^{-10}$–10^{-12} M) and are present largely in the form of ion pairs. The relevant data have been obtained by Streitwieser et al. for solutions of lithium and caesium cyclohexylamides in cyclohexylamine [131]. There is an important difference between the two salts. While caesium cyclohexylamide exists in cyclohexylamines in the form of monomeric ion pairs regardless of concentration [132], lithium cyclohexylamide also forms dimers, trimers, and other aggregates in equilibrium with the monomeric form [134,135].

The majority of metal salts of amino-compounds are extremely high-melting crystalline substances. It is somewhat surprising that the sodium salts of aniline and a number of other aromatic amines, obtained in liquid ammonia and then isolated in a pure form (judging from the results of elemental analysis), proved to be liquids [38].

There are apparently no literature data concerning the crystal structures of metal salts of amines. However, there are data on the structures of the crystal lattices of lithium [136] and sodium [137] amides. It is interesting that there are no hydrogen bonds in sodamide crystals. This is consistent also with the infrared spectrum of a crystalline specimen of sodamide, which contains sharp peaks at 3264 and 3218 cm^{-1}, associated respectively with antisymmetric and symmetric stretching vibrations of the N–H bonds, while bands which might be assigned to associated N–H groups are absent [59]. The infrared spectra of the potassium salt of methylamine [34] and the sodium salts of 5-aminoacridine and 2-amino-1-methylperimidine [59] are distinguished by similar characteristics, which indicates the absence of hydrogen bonds from their crystal lattices too. On the other hand, the spectra of the sodium salts of 2-aminopyridine and 1-alkyl-2-aminobenzimidazoles contain a number of diffuse bands in the region of N–H stretching vibrations, which is evidence of an appreciable association of the salts in the crystalline state.

Theoretically the nitrogen atom in the *N*-anions may be in the sp^3-, sp^2-, or *sp*-hybridised state:



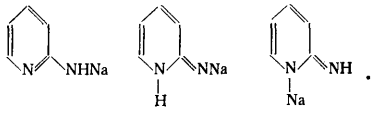
sp^3-hybridisation sp^2-hybridisation *sp*-hybridisation

Infrared spectroscopic data indicate a change in the state of hybridisation of the nitrogen atom in the *N*-anions compared with the parent amines. Thus the N–H stretching vibration band in the spectrum of potassium methylamide occurs at higher frequencies than in the spectrum of dimethylamine [34,138]. A similar phenomenon was observed for sodium salts of 5-aminoacridine and 1-alkyl-2-aminobenzimidazoles [59]. This probably indicates an increase of the *s*-character of the nitrogen hybrid orbitals and consequently of the force constant of the N–H bond on conversion of the amine into the corresponding metal salt. However, there are also exceptions to this rule [59].

In the infrared spectra of crystalline specimens of metal salts of methylamine and heterocyclic amines, almost all the bands characteristic of the initial amine are

retained with only a slight displacement. This must correspond to tight binding of the counterions in the crystal lattices of the salts, so that the negative charge remains largely localised on the nitrogen atom.

The similarity of the infrared spectra of the sodium salts of heterocyclic amines to those of the amines themselves led to the conclusion that in the crystalline state they exist in the amino-form (XXI) and not in the imino-forms (XXIa) or (XXIb):



(XXI) (XXIa) (XXIb)

Infrared spectra have been used successfully to elucidate the structures of arylmercury derivatives of nitro-, nitroso-, and azoaryl-amines [66,68].

Certain information concerning the characteristics of the structure of *N*-anions can be obtained also from ultraviolet spectroscopic data. Measurements have been made [9,12,13] of the ultraviolet spectra of a large series of sodium salts of anilines containing electron-accepting substituents and it was concluded, in particular, that the sodium salt of *p*-nitroaniline exists mainly in form (Xb). The ultraviolet spectrum of lithium cyclohexylamide has also been measured [36]. This salt (in cyclohexylamine) absorbs appreciably at 375 nm, which is at the boundary with the visible region.

The aromatic proton signals in the ^{1}H NMR spectra of the *N*-anions of aromatic amines, measured in liquid ammonia, are appreciably displaced towards higher fields compared with the unionised molecules, on average by 1 p.p.m. [22,23] The shift for different protons decreases in the sequence *para* > *ortho* > *meta*, which suggests an appreciable mesomeric interaction between the negatively charged nitrogen atom and the aromatic π-electron sextet.

There are also data for the electronegativities of the *N*-anions of aromatic amines in liquid ammonia solution [124,139].

II REACTIONS OF METAL SALTS OF AMINES

1. N-ANIONS AS STRONG BASES

Shatenshtein was the first to employ the KNH_2-NH_3 system to determine the kinetic acidity of C–H acids, including weak acids such as alkanes [140,141]. These studies stimulated the search for other *N*-anionic systems which might be used as suitable bases for the ionisation of weakly acid X–H bonds. The lithium (or caesium) cyclohexylamide–cyclohexylamine system, proposed and investigated in detail by Streitwieser [36,142] (see Ref. 143 for a review of Streitwieser's studies), has been recognised as one of the most successful. It was found that the ionising capacity of the cyclohexylamide anion depends on the type of metal cation [142]. For example, caesium cyclohexylamide in cyclohexylamine completely converts diphenylmethane and triphenylmethane into the carbanions, while the reaction with lithium cyclohexylamide does not go to completion and the following equilibrium is established:

$$\rangle C-H + C_6H_{11}NH^-Li^+ \rightleftarrows \rangle C^-Li^+ + C_6H_{11}NH_2 .$$

The higher reactivity (by a factor of 3300) of caesium cyclohexylamide in the ionisation of weak C–H acids can be accounted for in the first place by the monomeric nature of this salt in solution and in the second phase by the higher ionic radius of Cs^+ compared with Li^+. As a result, the Cs^+ ion is more remote from the $C_6H_{11}NH^-$ counterion, which enhances the reactivity of the latter.

Lithium di-isopropylamide (a Hünig salt) has found a wide-scale application as a deprotonating agent. Its advantages are due to the steric blocking of the *N*-anionic centre, which reduces to a minimum the probability of nucleophilic side reactions [144].

The 1,2,4-trihalogenobenzene → 1,2,5-trihalogenobenzene isomerisation in liquid ammonia, which involves a stage in which a C–H bond of the aromatic ring is deprotonated, proceeds most effectively in the presence of potassium anilide [63].

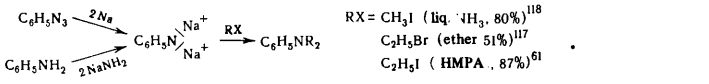
2. DEUTERIATION OF THE AMINO-GROUP VIA N-ANIONS

The amino-group is usually deuteriated by repeated refluxing of the amine in heavy water or in deuterio-alcohol [145]. For weakly acidic amines, deuterium exchange under these conditions is very slow. According to the results of the authors of this review, obtained for a series of *N*-heteroaromatic amines, and other data [101] for acid amides, a convenient method for the deuteriation of the NH_2 group consists in the decomposition of the metal salts of amines with heavy water (for a modification of this method, see Bassindale et al. [146]):

$$RN\bar{H}M^+ + D_2O \rightarrow RNHD + MOD,$$
$$RN^{2-}M_2^+ + 2D_2O \rightarrow RND_2 + 2\,MOD.$$

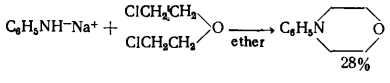
3. ALKYLATION

Many cases of alkylation of aromatic amines via *N*-anions have been described. For example, the aniline *N*-anions obtained from phenyl azide or aniline (by treatment with two moles of $NaNH_2$) give high yields of the corresponding *NN*-dialkylanilines with an admixture of the monoalkyl derivatives on alkylation with alkyl halides:



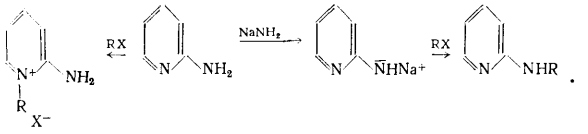
The preferential formation of the tertiary amine has been regarded as evidence for the involvement in the reaction of the disodium and not the monosodium salt of aniline.

Monosodium anilide is ethylated in ether at −40°C to monoethylaniline [38]. An unusual example of the employment of monosodium anilide is the following synthesis of *N*-phenylmorpholine [147]:



However, the alkylation of amines with a fairly active lone electron pair (these include aniline itself, aromatic amines with electron-donating substituents, and alkyl- and cycloalkyl-amines) can be carried out also without the preliminary ionisation of the N–H bond [148]. The alkylation of the amino-group via metal salts is important for amines with a reduced basicity, such as *p*-nitroaniline or 1-amino-1-phenylazonaphthalene.

Similarly the alkylation of the *N*-anions of tautomeric heterocyclic amines of the 2-aminopyridine type, is hardly the only practical method for the direct introduction of substituents into the NH_2 group. On the other hand, it is known that, when alkyl halides act directly on *N*-heteroaromatic amines, the reaction involves the endocyclic *N* atom:



When the NH_2 group is alkylated, it is important to be able to control the degree of reaction with formation of mono- or di-alkyl derivatives. The type of solvent employed is significant in this respect. In the alkylation of monosodium salts of aromatic or heteroaromatic amines in aprotic solvents of low polarity (aromatic hydrocarbons, ethers, dioxan), the reaction as a rule proceeds smoothly up to the formation of the corresponding monoalkyl derivative. In particular, derivatives of 2-aminopyridines with the following substituents in the NH_2 groups were obtained in this way: methyl [76], ethyl [140], propyl [150], isopropyl [149,151], butyl [150], isopentyl [149,152], cetyl [151], benzyl [153], diphenylmethyl [154], allyl [77,151], and dialkylaminoalkyl [78,155]. The interaction of the sodium salt of 2-aminopyridine with $\alpha\omega$-dihalogenoalkanes leads to $\alpha\omega$-dipyridylaminoalkanes [156]. Examples of such monoalkylation of the amino-group have been described for the 2-amino-derivatives of pyrimidine [78,81,147], quinoxaline [157], thiazole [80,158], lepidine [78,159], 1-alkylbenzimidazoles [71], and adenosine [160].

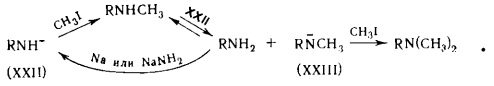
In order to rule out completely the possible formation of the dialkyl derivatives, in some cases the NH_2 group is first protected by formylation [161] or benzylation [59].

An attempt to obtain the dialkylamino-derivative by treating the monosodium salt of the amine with an excess of alkyl halide in a non-polar solvent usually leads to a complex mixture of substances containing not less than 50% of the tertiary amine [75]. Excellent results in the synthesis of dialkylamino-derivatives are obtained when liquid ammonia [71,82,83] or HMPA [82] are used as solvents.

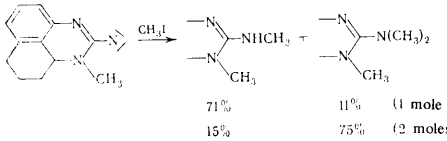
A remarkable characteristic of the reactions of the monoanions of aromatic and heteroaromatic amines with C_1-C_3 alkyl halides in liquid ammonia is that, regardless of the amine : alkyl halide ratio, the process does not stop at the monoalkylation stage [71,82]. Even in the presence of a deficiency of the alkyl halide, the corresponding dialkylamino-derivative is formed almost exclusively. The reaction is very fast with a high yield of the tertiary amine and undoubtedly constitutes the most convenient method of dialkylation of the amino-group. Similar results were obtained for the reaction of the *N*-anions of 4-aminoquinolines with halides of the allyl and benzyl type in HMPA [82].

The reaction of branched and more bulky (C_4 and above) alkyl halides with *N*-anions proceeds slowly snd gives mainly a low yield of the monoalkylation product [162]. It has been shown for aminoquinolines that γ-diethylaminopropyl chloride reacts with monoanions to form the monoalkyl-substituted derivative in nearly quantitative yield [87].

The preferential formation of the dialkylamino-substituted derivative on alkylation of monoanions with reactive alkyl halides in liquid ammonia and HMPA can probably be accounted for, as for the phenylacetonitrile carbanion [163], by the stepwise nature of the reaction. Of the two types of monoanions, (XXII) and (XXIII), present in solution, (XXIII) is probably alkylated at a rate which greatly exceeds that of (XXII). Therefore, despite the low equilibrium concentration of (XXIII), the dialkylamino-derivative and not the monoalkyl-amino-derivative accumulates continuously in the reaction mixture:



In contrast to the monoanions, the alkylation of the dianions in liquid ammonia is susceptible to definite control and, depending on the amount of the initial alkyl halide, the reaction can be directed towards the preferential formation of the mono- or di-alkyl derivative [71]:



This behaviour of the dianions is quite reasonable, since their reactivity should be higher than that of the monoanion of a secondary amine. As a result, the secondary amine, the alkylation of which becomes significant only after the disappearance of the dianion or a sharp decrease of their concentration, accumulates in the reaction mixture. The existence in solution of a particular anionic species has been frequently inferred in the literature from the results of alkylation experiments.

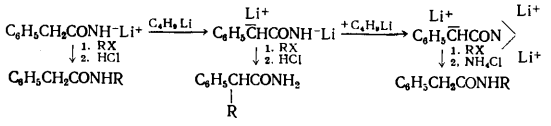
It follows from the foregoing data that the formation of the dialkyl derivative when an excess of alkyl halide acts on the *N*-anions of aniline and other amines in liquid ammonia [118] (and also in HMPA) cannot be regarded as unambiguous proof of the presence of dianions in solution. The same results might be obtained by the alkylation of the corresponding monoanions in the same solvents. It is more correct to employ as a basis the results of the alkylation of the *N*-anions by one equivalent of methyl iodide [71]. In this case the preferential formation of the dimethylamino-derivative should be regarded as evidence of the formation of the monoanion in solution and the formation of a secondary amine should indicate the presence of the dianion. The use of this test for the *N*-anions of 2- and 5-aminobenzimidazoles obtained from the corresponding azides [71] showed that the dianions, formed initially in liquid ammonia, are appreciably ammonolysed to the monoanions. Bearing in mind the low acidity of aniline, it is unlikely that its dianion, obtained from phenyl azide, is stable in liquid ammonia and does not undergo ammonolysis.

Incidentally, this test is not universal. It has been found that the monoanions of acidic amines capable of forming dianions simply on treatment with sodium, are not susceptible to stepwise alkylation in liquid ammonia and, on treatment with one mole of methyl iodide, form preferentially the monoalkylation product [71]. However, the identification of the *N*-anions of such amines presents no difficulties even without alkylation, since the very fact of their conversion into dianions on treatment with sodium is evidence of the stability of both their monoanions and dianions in liquid ammonia.

An interesting feature of the alkylation of the *N*-anions of heteroaromatic and aromatic amines consists in the fact that, despite their formal ambident nature [see, for example, structures (XXI) and (XXIb)], the reaction involves exclusively the amino-nitrogen, i.e. takes place

without transfer of the reaction centre. This indicates an appreciable localisation of the negative charge on the exocyclic N-atom not only in the isolated but also in the reacting molecule.

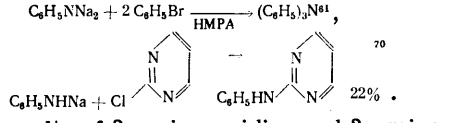
If the molecule contains several anionic centres, the centre formed last, i.e. the one to which corresponds the less acidic X—H bond, is the first to be alkylated [99,101]:



Less nucleophilic and hence less reactive N-anions correspond to acid amides as well as N—H acids stronger than amines. The alkylation and benzylation of the sodium salts of carboxylic acid amides in liquid ammonia [164], HMPA, [61] or non-polar aprotic solvents [165,166] takes place slowly and leads to the formation of N-monosubstituted derivatives in low yields. The sodium salt of urea does not react in liquid ammonia with butyl and dodecyl bromides, but monobenzylurea is formed by the reaction with benzyl chloride [106].

4. ARYLATION

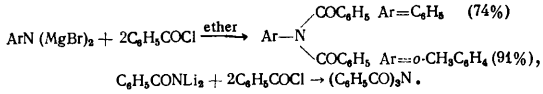
The arylation of the amino-group and the introduction of heterocyclic substituents into it via the N-anions usually take place slowly and require heating of the reactants for many hours in a high-boiling solvent or even without a solvent. The yields of reaction products are as a rule low. Characteristic examples are provided by the following reactions:



The sodium salts of 2-aminopyridine and 2-aminopyrimidine interact with 2-chlorothiazole to form 2-(α-thiazolylamino)-derivatives in yields of 40 and 9.5% respectively [70]. The reaction of the sodium salt of 2-aminopyrimidine takes place only in the absence of solvent, which can be accounted for by its lower nucleophilicity compared with the N-anion of 2-aminopyrimidine.

5. ACYLATION

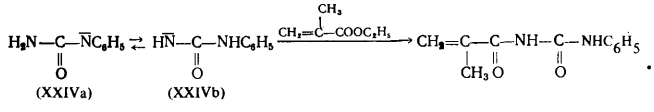
The acylation of the amino-group via metal salts is usually achieved with the aid of carboxylic acid chlorides or esters. The use of the latter leads to monoacyl derivatives regardless of whether the mono- or di-anion is introduced into the reaction. When acid chlorides act upon monometal salts, monoacylation products are also formed, but with dimetal salts high yields of NN-diacyl derivatives can also be obtained. Examples of reactions of this kind are known for both a series of amines [55,167–169] and a series of acid amides [101]:



It is noteworthy that mainly the diacylation of the NH_2 groups via N-anions is of preparative importance, since almost all amines can be readily monoacylated as such with the aid of acid anhydrides or chlorides. On the other hand, the acylation of a second N—H bond in the monoacyl derivative formed is much more difficult without its conversion into the N-anion.

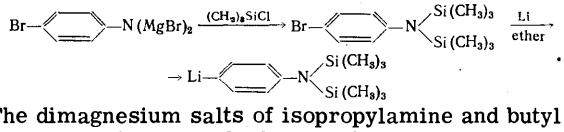
In only a few cases, when the acid chloride or anhydride is difficult to obtain or cannot be employed for one reason or another, the use of esters for the monoacylation of the amino-group also assumes synthetic importance. A characteristic example is provided by the acylation of aromatic amines via magnesylamines with the aid of ethyl β-hydroxy-$\beta\beta$-diphenylpropionate [168]. As might have been expected, dimagnesylamines are more reactive in this process [55].

The monosodium salts of urea and N-phenylurea are acylated in liquid ammonia or acetone with the aid of acid chlorides or esters [106], including ethyl methacrylate [169], to give the corresponding monoacyl derivatives. It is interesting that the reaction with N-phenylurea involves the primary amino-group, although the N-anion (XXIVa) and not (XXIVb) should be more stable in this case. Probably the anion (XXIVb), although present at a low concentration, reacts with the acylating agent much faster than does (XXIVa):



6. REACTION OF N-ANIONS WITH CHLOROTRIMETHYLSILANE

Magnesium [56,57] and lithium salts [146] of aromatic amines react under mild conditions with chlorotrimethylsilane, giving a high yield of the corresponding trimethylsilyl derivatives. The reaction has been used to protect the amino-group in organometallic syntheses [57,170]:



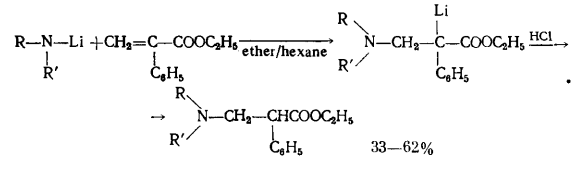
The dimagnesium salts of isopropylamine and butylamines do not form N-alkylhexamethyldisilazanes on treatment with chlorotrimethylsilane. However, the lithium salts of alkylamines, for example of t-butylamine [36] and N-phenylethylenediamine [171], react readily under these conditions.

7. NUCLEOPHILIC ADDITION OF N-ANIONS TO MULTIPLE BONDS

Compared with amines, N-anions are much more nucleophilic and add more readily to polarised multiple bonds. This factor is very widely used in organic synthesis.

a. Addition to Carbon—Carbon Multiple Bonds

Reactions of this type have been little investigated. It has been found that lithium salts of secondary amines add to the C=C bond of ethyl α-phenylacrylate according to the following mechanism [172]:



The mode of this reaction is the opposite of that of primary amine *N*-anions with ethyl methacrylate in which there is addition to the C=O bond followed by acylation of the amino-group.

Sodium anilide adds to the triple bond of dehydrobenzene, yielding *N*- and *C*-arylation products: diphenylamine, 2-aminobiphenyl, and 4-aminobiphenyl[173]. The formation of biphenyl derivatives in this reaction clearly demonstrates the ambident nature of the aniline *N*-anion.

b. Addition to the C=O bond

One of the examples of such reactions may be the carboxylation of the diphenylmethylamine *N*-anion by carbon dioxide leading to the formation of diphenylmethylcarbamic acid, as already mentioned above. The acylation of the amino-group via the *N*-anion by carboxylic acid esters also includes a stage involving addition to the C=O bond and constitutes another example of this kind.

It has been shown recently that the *N*-anions of primary amines add to the triple bond of carbon monoxide[174]. The lithium salt of t-butylamine gives rise to orange t-butylcarbamoyl-lithium (XXV):

$$(CH_3)_3CNH^-Li^+ + \bar{C}\equiv\overset{+}{O} \rightarrow (CH_3)_3CNH-\underset{\underset{O}{\|}}{C}-Li$$

(XXV)

Many condensation reactions involve as an intermediate stage the formation of an *N*-anion, which behaves as an active species and adds directly to the carbonyl group. Such reactions include, in particular, the hydroxymethylation of carboxylic acid amides by formaldehyde in an alkaline medium[175].

Although the Schiff reaction is known to be usually catalysed by acids, cases of base catalysis have also been noted for amines with an inactive electron pair at the nitrogen atom. For example, 2-aminobenzimidazoles react with aldehydes of the furan series in the presence of alkali much more readily than in its absence[176]. Bearing in mind the enhanced acidity of the N–H bonds in such amines, there can be hardly any doubt that the species involved in such reactions is not the amine itself but the *N*-anion in equilibrium with it:

$$RNH_2 + OH^- \rightleftharpoons RNH^- + H_2O \xrightarrow{R'CHO} R-N(H)-CH(O^-)-R' \longrightarrow R-N=CH-R' + OH^-$$

It has been suggested that *N*-anions participate also in the complex Marschalk reaction in which the sodium salts of the leuco-derivatives of aminoanthraquinones are acted upon by aldehydes[177] with formation of *C*-alkylated aminoanthraquinones.

c. Addition to the C≡N Group

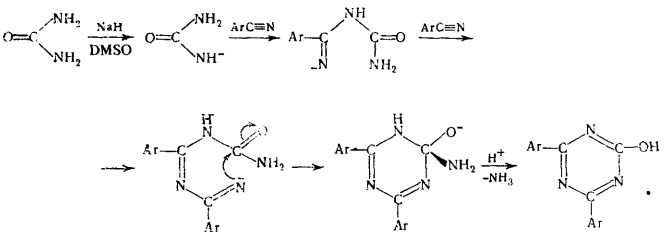
The addition of metal salts of amines to the C≡N bonds of nitriles constitutes the basis of one of the simplest methods for the synthesis of substituted amidines:

$$RNH^-M^+ + R'C\equiv N \rightarrow R'-C(=NM)-NHR \xrightarrow{HCl} R'-C(=NH)-NHR$$

Although this reaction has been known for a long time[2,178,179], it was not investigated in detail and for a large number of examples until 1970.[180] It was shown that the most suitable solvent for the process is liquid ammonia. The reaction then proceeds much faster and with a higher yield of amidine than in non-polar aprotic solvents. Good results are apparently obtained also in DMSO.[181]

However, only aromatic and heteroaromatic amines and nitriles enter into this reaction. The reaction with alkylamines (n-$C_4H_9NH_2$) takes place with a low yield or not at all (iso-$C_3H_7NH_2$). Somewhat better results were obtained for benzylamine and diphenylmethylamine. When these are acted upon by potassamide in liquid ammonia with subsequent introduction of benzonitrile, the yields of the substituted amidine are 29 and 73% respectively[180]. All these results apparently reflect the relative acidity of the N–H bonds in amines and the ease of formation by them of *N*-anions in liquid ammonia.

The interaction of the *N*-anion of urea and aromatic nitriles in DMSO is unusual. The product of the two-stage process is a 2-hydroxy-4,6-diphenyl-*s*-triazine[181]:



d. Addition to the N=O Bond

Aromatic amines, in particular aniline, are readily condensed with nitrobenzene and its derivatives in the presence of strong bases (for example t-BuOK in DMSO), yielding the corresponding azo-compounds[182–184]. The role of the base consists in the conversion of the amine into the *N*-anion, which is more reactive in relation to the nitroso-group:

$$ArNH_2 + B^- \rightleftharpoons ArNH^- + BH \xrightarrow{Ar'N=O} Ar-N(H)-N(O^-)-Ar' \longrightarrow Ar-N=N-Ar' + OH^-$$

This reaction is very important in the series of *N*-heteroaromatic amines which are otherwise difficult to convert into azo-compounds, since the amino-group is diazotised with difficulty and the corresponding diazonium salts are extremely unstable. Such amines include, for example, α- and γ-amino-derivatives of pyridine[72,73,79,185], quinoline[72], and benzimidazole[186].

A similar type of reaction constitutes the basis of the method proposed by Bamberger and Rust for the diazotisation of aromatic amines[187]. In this procedure, the aromatic amine is treated with pentyl nitrite in the presence of an alkali metal alkoxide, which results in the formation of the corresponding diazotate:

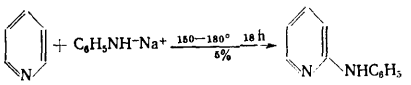
$$ArNH_2 + C_2H_5O^- \rightleftharpoons C_2H_5OH + ArNH^- \xrightarrow{C_5H_{11}ONO} Ar-N(H)-N(O^-)-OC_5H_{11} \longrightarrow$$

$$\longrightarrow Ar-N=N-O^-Na^+ + C_5H_{11}OH$$

Chichibabin showed for 2-aminopyridine that the sodium salt of the amine beforehand can also be introduced into the Bamberger reaction[188].

8. ALKYL- AND ARYL-AMINATION OF ORGANIC COMPOUNDS WITH THE AID OF N-ANIONS (REACTIONS WITH ELIMINATION OF THE HYDRIDE ION)

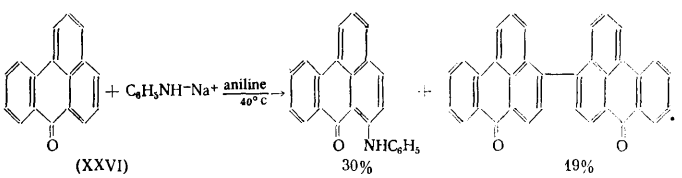
By analogy with the amination of nitrogenous heterocycles with sodamide (Chichibabin reaction)[189], it is very tempting to employ for the same purpose organic derivatives of sodamide. Chichibabin[190] already found that sodium anilide reacts with pyridine under severe conditions to form an insignificant amount of 2-phenylaminopyridine:



The formation of 2,2′-dipyridylamine as a side product in the reaction of pyridine with sodamide was also accounted for by the reaction of pyridine with the sodium salt of 2-aminopyridine formed as a result of amination[190,191].

However, on the whole the salts of aromatic amines are not sufficiently nucleophilic in relation to *N*-heterocyclic compounds and the yields of amination products are extremely low. Even more frequently, the reaction does not proceed at all, for example with quinoline[192] and isoquinoline[193] or when pyridine is acted upon by sodium *N*-methylanilide[194].

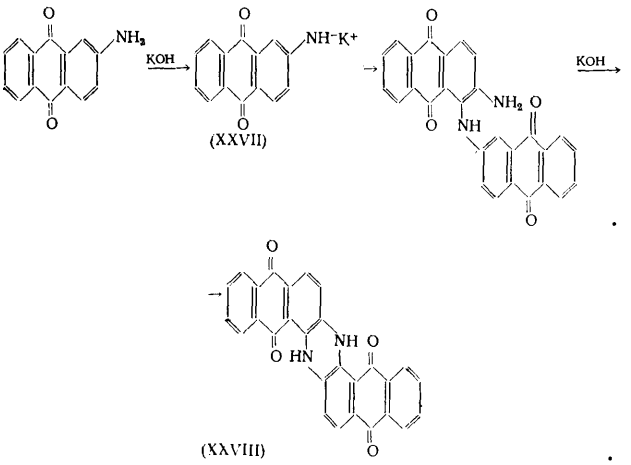
Phenylamination with the aid of sodium anilide takes place somewhat more readily in the series of certain polynuclear systems: mesobenzanthrone (XXVI),[195,196] 1,8,9-naphthanthr-10-one,[197] 1,9-pyrazolanthrone[60], and 1,8-naphthalimide[198]. Bradley, who made a detailed study of these reactions[196-199], showed that in all cases two competing processes take place—direct phenylamination and dimerisation of the initial compound:



(XXVI) 30% 19%

Bradley assumed that the dimerisation reaction is due to the ionisation of the C–H bond in the molecule of the initial compound under the influence of $C_6H_5NH^-Na^+$ with subsequent addition of the carbanion formed to another molecule of the initial compound[196]. However, bearing in mind that dimers are formed also when the above polynuclear compounds are acted upon by metal alkoxides in alcohol or by alkalis, which can hardly cause the ionisation of aromatic C–H bonds under the reaction conditions, a reductive dimerisation mechanism is more likely: electron transfer from the base to the aromatic substrate, cross-linking of the two radical-anions formed, and subsequent oxidation of the dihydro-derivative of the dimer to the aromatised dimer. The amination and dimerisation processes compete with one another also in the Chichibabin reaction (the reaction of sodamide with *N*-heteroaromatic compounds). It was shown recently that dimerisation in the Chichibabin reaction proceeds most probably via a stage involving the formation of a carbanion[90].

When β-aminoanthraquinone is heated with potassium hydroxide in pyridine or in the absence of solvent, the resulting *N*-anion (XXVII) can enter into a nucleophilic interaction with a molecule of the initial compound[199]. Ultimately this reaction leads to the formation of the dye indanthrone (XXVIII):[200]

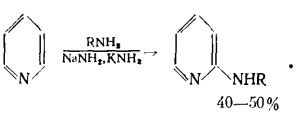


(XXVII) (XXVIII)

The *N*-anion (XXVII) also adds to nitrobenzene[199]. The more readily formed but less nucleophilic *N*-anions of 2-amino-1-chloro- and 2-amino-1-nitro-anthraquinones do not react with nitrobenzene[199].

One may suppose that the reactivity of metal salts of alkylamines as nucleophilic agents should be greater. However, there are very few data concerning this problem. Thus, when quinoline is acted upon by sodium methylamide in ether, it forms 2-methylaminoquinoline (yield not stated)[201,202]. Alkali metal dialkylamides do not react at all (even when the conditions are altered) with nitrogenous bases or cause charring[193,201,203].

Bergstrom et al. succeeded in alkylaminating pyridine and quinoline in the 2-position by treating them with a eutectic mixture of sodamide and potassamide in the presence of primary aliphatic or alicyclic amines and potassium nitrate[204]:



40–50%

Kovacs and Vajda modified this method, having replaced the eutectic mixture of the two amides by metallic sodium[205-208]. Both groups of investigators failed to obtain evidence for the involvement in this reaction of the alkylamine *N*-anion as a nucleophilic agent (on the basis of the absence of visible signs of interaction between the amine and the base) and therefore the problem of its mechanism remains open. However, it is difficult to imagine a mechanism for this reaction other than one involving the alkylamide anion. It is likely that the formation of even a small equilibrium amount of the metal salt of the amine (it is quite possible under the reaction conditions) followed by its interaction with heterocyclic compounds gradually displaces the amine ⇌ *N*-anion equilibrium to the right.

The majority of alkyl- and aryl-amination reactions involving *N*-anions are not accompanied by the evolution of hydrogen, in contrast to the Chichibabin reaction. To eliminate the hydride ion from the intermediate σ-complex, oxidising agents must be employed: potassium nitrate, air, or pure oxygen.

9. OXIDATION REACTIONS OF N-ANIONS

In general *N*-anions are oxidised much more readily than the neutral amines. Most data have been obtained for the autoxidation reaction. The reactivity of metal salts of amines in relation to molecular oxygen may be extremely varied: ranging from nitroarylamine and 2-amino-pyrimidine salts, which are completely stable in air, to metal salts of alkylamines which react vigorously with oxygen. Thus less reactive amines give rise to more readily oxidised *N*-anions and conversely.

Sodium anilide and metal salts of arylamines with electron-donating substituents rapidly blacken in air and are converted into a mixture of high-molecular-weight autoxidation products. A controlled and mild autoxidation of the *N*-anions of aromatic amines to azo-compounds has been achieved in the NaH–THF,[52] t-C_4H_9OK–toluene[209], and t-C_4H_9OK–DMSO[183,184,210] systems. Two views have been expressed concerning the mechanism of this reaction. According to the first, on being acted upon by oxygen, the *N*-anion is converted into a radical (**XXIX**), which dimerises to the corresponding hydrazobenzene. The latter is then transformed (also via the *N*-anion) into azobenzene[209]:

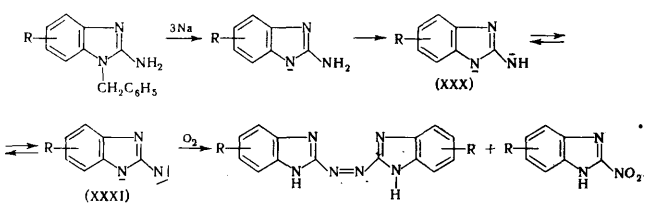
$$ArNH_2 + t\text{-}C_4H_9OK \rightleftarrows ArNH^-K^+ + t\text{-}C_4H_9OH,$$
$$2\,ArNH^-K^+ + O_2 \rightarrow 2\,ArNH + O_2^-,$$
(XXIX)
$$2\,\mathbf{XXIX} \rightarrow ArNH{-}NHAr \rightarrow Ar\overset{K^+}{N}{-}\overset{K^+}{N}Ar \xrightarrow{O_2} Ar{-}N{=}N{-}Ar + K_2O_2.$$

This mechanism probably obtains in many cases (see, for example, Filipskikh et al.[120]), but, as shown recently[182,210], the reaction involving aniline itself and its substituted derivatives proceeds via a different pathway involving the condensation of an intermediate nitroso-compound with the amine *N*-anion.

The *N*-anions of α- and β-aminoanilines form dibenzo[*a*,*h*]phenazine on oxidation with oxygen[209].

The monoanions of 2-amino-derivatives of pyridine, benzimidazole, thiazole, and other nitrogenous heterocycles react very slowly with oxygen. Usually the corresponding azo-compound is formed in low yields under these conditions[91]. An exception is the monoanion of the less acid 2-amino-4,5-diphenylimidazole, which readily oxidises in air to 2,2′-azoimidazole[91].

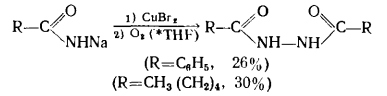
The polyanions of 2-aminobenzimidazole and certain other 2-aminoimidazoles exhibit an unusually high reactivity in the autoxidation reaction for reasons which are not obvious[91]. It was found that the polyanions (**XXX**) and (**XXXI**), formed on debenzylation of 2-amino-1-benzylbenzimidazoles with sodium or potassium in liquid ammonia, react rapidly with atmospheric oxygen at temperatures as low as −70°C, being converted quantitatively into a mixture of 2,2′-azo- and (unexpectedly) 2-nitrobenzimidazoles[91,211,212]:



This reaction is the only known example of such ready autoxidation of the amino-group to the nitro-group.

The polyanions (**XXX**) and (**XXXI**) can also be obtained from 2-azido-,[119] 2-benzylamino-,[126] 2-amino-1-arylalkyl-,[90] and 2-amino-benzimidazoles.[91] The attempts to drive the autoxidation process towards the preferential formation of the more valuable 2-nitrobenzimidazole (analogue of the antibiotic azomycin) have so far remained unsuccessful: the maximum yield of the nitro-derivative achieved does not exceed 45%. The mechanism of the formation of 2-nitrobenzimidazole is still obscure; however, it has been established that the reaction is influenced by a series of factors: the type of the imidazole system, the nature of the solvent, the metal, the substituent at $N_{(1)}$, the method of generation of the *N*-anion, and others. For example, the trilithium salt of 2-aminobenzimidazole is oxidised by oxygen in ether only as far as 2,2′-azobenzimidazole (yield 90%).

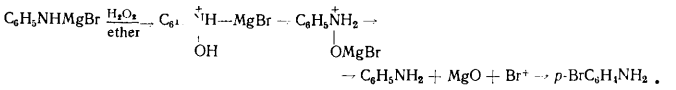
It has also proved possible to achieve the oxidative dimerisation of metal salts of acid amides and amidines. It was found that copper salts of N–H acids are oxidised by oxygen much more readily than the sodium or lithium salts[213]:



It is remarkable that copper(I) chloride catalyses (also, it is believed, via the formation of a copper salt) the autoxidation of aniline to azobenzene in pyridine solution[214,215].

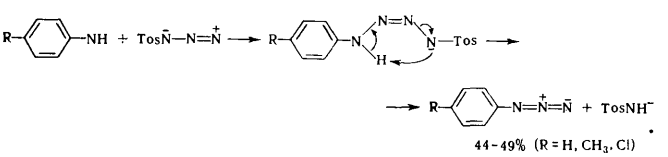
The oxidation of *N*-anions by other oxidising agents has been little studied. The anions of certain *N*-heteroaromatic amines (triazoles[216,217], benzothiazoles[218], and benzimidazoles[120,219]) are oxidised by $KMnO_4$, $K_2S_2O_8$, and NaOCl to the corresponding azo-compounds, the reaction being of preparative value in some cases.

When hydrogen peroxide in ether is allowed to react with the bromomagnesium salt of aniline, *p*-bromoaniline[220] (and not phenylhydroxylamine as reported earlier[221]) is formed. The mechanism proposed for this reaction involves the intermediate formation of positively charged bromine[220]:



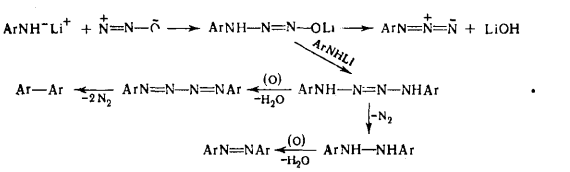
10. OTHER REACTIONS OF N-ANIONS

An unusual conversion of amine *N*-anions into azides with the aid of *p*-toluenesulphonyl azide (TSA), which plays the role of a diazo-transferring agent, was discovered by American workers[222]. The reaction is believed to proceed via a triazene intermediate and reduces in the initial stage to the addition of the *N*-anion to the azido-group of TSA in one of its resonance forms with the positive charge at the terminal nitrogen atom:

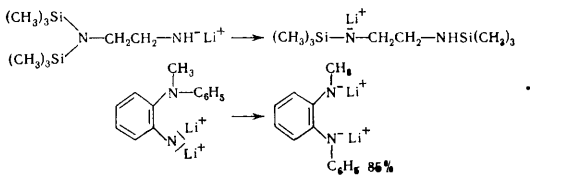


The *N*-anion of benzylamine has been converted into benzyl azide in a yield of 26%. The less nucleophilic *N*-anions of acid amides and *p*-nitroanilines could not be converted into azides in this way.

The interaction of the *N*-anions of amines with nitrous oxide[53,54] is closely related to the above reaction. However, in this case the yield of the azide does not exceed 10–35%. The corresponding biphenyl and azobenzene, which is the main reaction product, are also formed[54]. In general, the processes can be represented as follows:

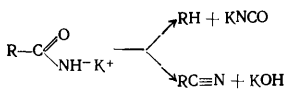


In a study of *N*-anionic rearrangements in the series of asymmetric hydrazines, West observed that to some extent they are characteristic also of the *N*-anions of aromatic and aliphatic diamines. The following two examples illustrate the 1,4-anionic rearrangements of this type[170,223]:

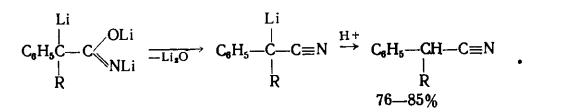


It is remarkable that in the case of *o*-aminobiphenylyl-*N*-methylamine, only the dianion undergoes a rearrangement[223].

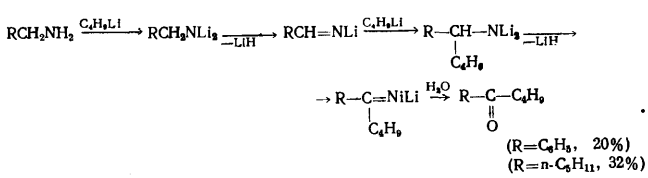
Elimination reactions with conversion into nitrile and certain other compounds are characteristic of the *N*-anions of many acid amides. For example, the potassium salts of formamide and urea decompose extremely readily with formation of potassium cyanate and the evolution of hydrogen and ammonia respectively[224]. The *N*-anions of other amides of aliphatic[224] and aliphatic-aromatic[100] acids decompose on heating via two pathways—with formation of a hydrocarbon and a nitrile:



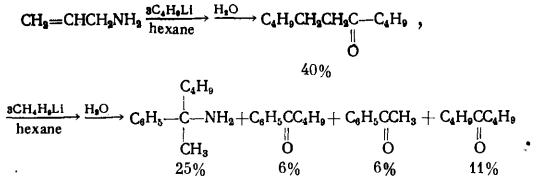
Hauser and coworkers used this property of the *N*-anions of acid amides for preparative purposes. They established that the trianions of aryl- and diaryl-acetamides are converted under mild conditions into the corresponding nitriles in high yields[98,99]:



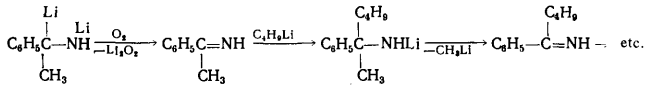
Interesting reactions of the dilithium salts of primary alkyl- and arylalkylamines were discovered recently[225]. On refluxing in hexane in the presence of an excess of butyl-lithium and subsequent hydrolysis, the dilithium salts of alkylamines yield ketones with a butyl group. The authors suggested that the reaction proceeds according to the following elimination–addition mechanism



The reaction involving allylamine and α-phenylethylamine proceeds in a more complex manner:



Unfortunately the question of the possible ionisation of the C–H bond in the methine group of α-phenylethylamine was not investigated in the study quoted above. In the light of what has been said earlier concerning the metallation of CH–NH systems (p.39), this is a very likely possibility and the formation of all the products enumerated could be predicted theoretically also on the basis of the conversion of the *CN*-dianion:



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Interesting studies on the gas-phase acidity of alkyl- and dialkyl-amines[226] and on the synthesis of substituted acid amides from esters and sodium salts of aryl- and cycloalkyl-amines[227] were published recently.

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Rostov-on-Don State University

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Dual Reactivity of Arylmethylmetal Compounds

D.V.Ioffe and M.I.Mostova

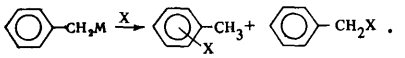
The review deals with the dual reactivity of ambident anions of arylmethylmetal compounds. Data on the mechanism of reactions of these compounds are described and the effect of various factors on the mode of reaction is discussed. The bibliography includes 93 references.

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I. INTRODUCTION

The reaction of benzylmagnesium chloride with trioxymethylene leading to the formation of β-phenylethyl alcohol was described in 1903.[1] In the same year it was reported[2] that the product of this reaction is *o*-tolylmethanol and that benzylmagnesium chloride therefore exhibits dual reactivity in its reaction with trioxymethylene:



The first stage in the study of the dual reactivity (or the so called "anomalous" reaction of arylmethylmetal compounds) was the determination of the generality of the reaction. It was found that, together with organomagnesium compounds, arylmethyl derivatives of other Group I (potassium[3], sodium[4], and lithium[5]), Group II (zinc[6-8], cadmium[6], and mercury[9,10]), and Group III (aluminium[6] and boron[11-14]) metals react similarly. The dual reactivity was observed not only in relation to carbocyclic but also heterocyclic compounds, namely derivatives of furan[15], thiophen[16-18], and their benzo-analogues[19]. The range of electrophilic reagents entering into the aromatic ring proved to be extremely wide, including aldehydes, ketones, various acid derivatives (esters, nitriles, anhydrides, and acid halides), carbonic acid derivatives (carbon dioxide, ethyl chlorocarbonate, phosgene, dicyanogen, and dithiocyanogen), alkyl halides, sulphuric acid esters, deuterium chloride, heavy water, etc. It was found that, together with the more usual *ortho*-substitution, in many cases *para*-substitution takes place and in a few reactions this is in fact the dominant process.

Some of the data obtained up to 1954 and dealing with reactions of organomagnesium compounds are summarised in Chapter XI of the monograph by Kharash and Reinmuth[20], who quote exhaustive factual data and put forward certain hypotheses concerning the reaction mechanism. Then, for a time, the reaction was hardly investigated. In the monograph by Ioffe and Nesmeyanov[21], only two isolated special studies[22,23] were added to those discussed in the previous review[20]. However, in recent years, interest in this reaction has been renewed, as can be seen from a considerable number of investigations dealing with the dual reactivity of arylmethyl compounds of both magnesium and other metals. The data which have now accumulated permit a general account of the dual reactivity of arylmethylmetal compounds and the determination of the general characteristics of the relevant reaction and of the effect of various factors on its course. The present review is an attempt at a general account of this kind.

II. REACTION MECHANISM

Tiffeneau and Delange, who were the first to describe the dual reactivity of benzylmagnesium chloride, already stated [referring to the corresponding reaction] that "this is a condensation of the same type as in the formation of primary aromatic alcohols by the reaction of formaldehyde with arylhydroxylamines or sodium phenoxide"[2]. In fact all investigators treat unamimously the "anomalous" reaction of arylmethylmetal compounds as a special case of electrophilic substitution in the aromatic ring activated as a result of the conjugation of the electrons of the carbon–metal σ-bond and the ring π-electrons†[24]. This conjugation accounts for the unusually high (compared with the effect of the methyl group) electron-donating effect of the CH_2M group, which is comparable to that of powerful electron-donating agents such as the amino- and hydroxy-groups (Table 1). The σ-π conjugation in the molecules of arylmethylmetal compounds explains their capacity to form *ortho*- and *para*-substitution products, but does not account for the finding that *ortho*-isomers predominate in the reaction products. Moreover the main product of the reactions of arylmethylmetal compounds is the *ortho*-isomer and the formation of the *para*-isomer may be regarded as exceptional. Selective *ortho*-substitution has been the starting point of the study of the reaction mechanism. Different related mechanisms, proposed to account for the dual reactivity of organomagnesium compounds[25-30], can be represented in a general form by Scheme 1 (c.f. Kharash and Reinmuth[20]) using as an example the interaction of benzylmagnesium chloride with formaldehyde.

Table 1. σ⁺ constants of the substituents[14,27].

Substituent	σ+	Substituent	σ+
Me	—0.311	CH_2HgCH_2Ph	—1.14
OH	—0.92	NH_2	—1.3
$CH_2\bar{B}X_2OH$*	—1.11		

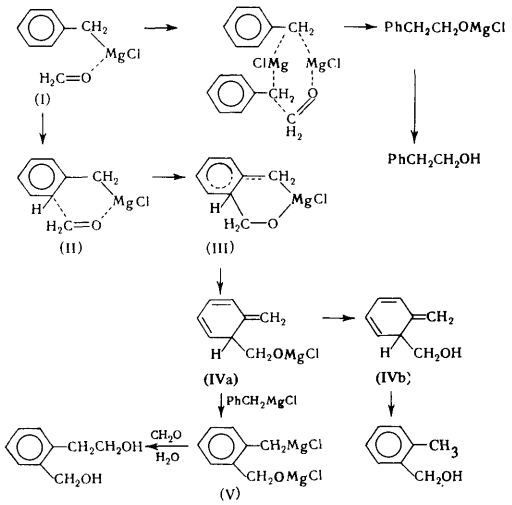
* X = acid residue

†The discussion which arose between Schmidlin[25], who attempted to justify the existence of two isomeric forms of benzylmagnesium compounds, and Chichibabin[26], who supported the idea of a dual reactivity of this compound, is of historical interest.

The first stage of the reaction is the formation of a Werner complex (I), which can react with a further molecule of benzylmagnesium chloride to form a quasi-six-membered ring, the decomposition of which leads to phenylethyl alcohol.

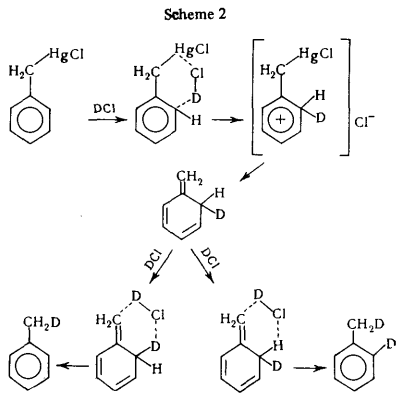
To account for the "anomalous" course of the reaction, one postulates the formation of an oriented π-complex (II), which is subsequently transformed into a σ-complex (III) and then into an *o*-metallated derivative of methylenecyclohexadiene (IVa). Hydrolysis of the latter results in the formation of methylenecyclohexadiene (IVb) the aromatisation of which leads to the final *ortho*-substitution product. Methylcyclohexadiene (IVa) can be metallated by an excess of the organomagnesium compound to form a new organomagnesium compound (V), which again reacts with formaldehyde.

Scheme 1



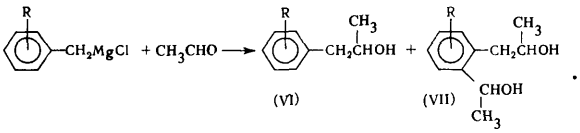
A similar scheme was proposed[31] to account for the dual reactivity of benzylmercury chloride (see Scheme 2).

Scheme 2



One must suppose that similar mechanisms can be put forward to account for the dual reactivity of the arylmethyl derivatives of other metals too. Scheme 2 is close to the mechanisms of electrophilic aromatic substitution reactions, for example the Kolbe reaction or the reaction involving the *ortho*-hydroxymethylation of phenols.

The individual stages of the proposed mechanism have been examined in various investigations and their occurrence with formation of intermediates has been demonstrated. Thus the formation of the oriented π-complex (II) as an essential stage in the formation of *ortho*-substituted products has been elegantly confirmed by Bernardon and Bourdais[32], who investigated the reaction of acetaldehyde with substituted benzylmagnesium chlorides:

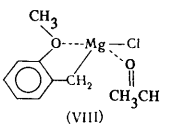


The reaction resulted in the formation of both the normal addition product, the secondary alcohol (VI), and of the "anomalous" diol (VII). The ratio of the yields of these products depends on the nature and position of the substituent in the phenol ring (Table 2).

Table 2. Effect of the substituent on the yield of products of the reaction of benzylmagnesium chloride and acetaldehyde.

Compound	R	Yield, %	Compound	R	Yield %
VI	H	10	VII	H	50
	o-OMe	70		*o*-OMe	0
	p-OMe	12		*p*-OMe	45
	o-Me	0		*o*-Me	85

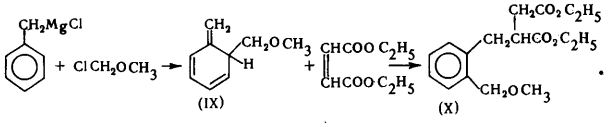
In the reaction involving *o*-methoxybenzylmagnesium chloride, the ring *ortho*-substitution product is not formed. Comparison with the reactions of *p*-methoxy- and *o*-methylbenzylmagnesium chlorides does not explain this phenomenon on the basis of the electronic or steric effects of the *o*-methoxy-group. The authors believe that the complex (I) formed in the reaction with *o*-methoxybenzylmagnesium chloride has structure (VIII), which rules out the formation of a π-complex and an *ortho*-substitution product.



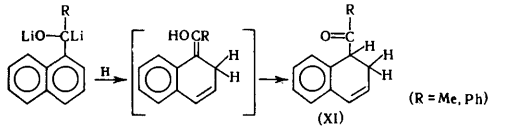
On the other hand, the steric effect of the *ortho*-methyl group favours the formation of a π-complex, the absence of the alcohol (VI) from the products being related to this factor. It is interesting to note that at an even earlier stage the absence of dual reactivity in ferrocenylmethyllithium was attributed to the impossibility of the formation of a cyclic transition state[33].

The formation of methylenecyclohexadiene in the course of reactions of arylmethylmetal compounds has been frequently postulated. The formation of considerable and sometimes predominant amounts of diaddition products is always explained by its presence. Bearing in mind the stability of methylenecyclohexadiene itself[34], its formation in the course of the reaction appeared extremely probable. Convincing proof of this was obtained[35-37]. In order to detect the methylenecyclohexadiene derivatives formed in the course of the reaction of benzylmagnesium chloride,

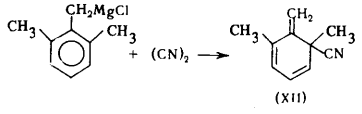
active substances, capable of reacting with these intermediates, were added to the reaction mixture. Thus the reaction mixture, obtained by allowing benzylmagnesium chloride to react with α-chloromethyl ether, was treated with diethyl maleate or maleic anhydride. The detection of diethyl α-(*o*-methoxymethylbenzyl) succinate (X) proved the existence of compound (IX):



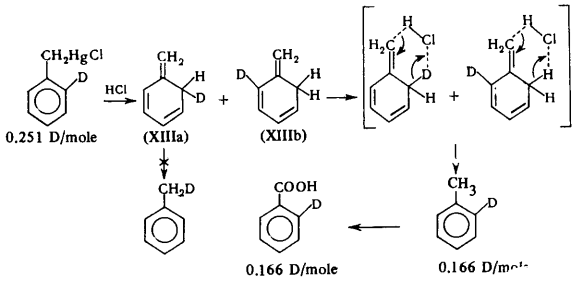
In a few cases, when the compounds with the methylenecyclohexadiene structure are stablised by additional factors, their formation may be demonstrated by spectroscopic methods. Thus, when α-hydroxyarylmethylmetal compounds of the naphthalene series were protonated, the formation of the diene system (XI) was demonstrated[38]:



Finally, compound (XII), formed in the reaction between 2, 6-dimethylbenzylmagnesium chloride and dicyanogen, was isolated[39]:

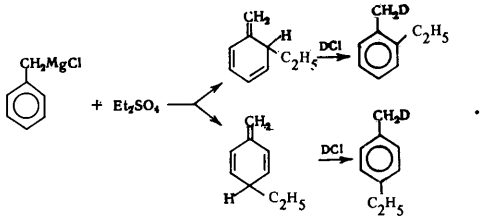


The data presented confirmed the hypothesis of the formation of methylenecyclohexadiene compounds in the course of the reaction. The problem of the aromatisation of the intermediates is somewhat more complex. At first sight it may appear that the simplest aromatisation pathway involves intramolecular proton migration. However, Kharash already pointed out that the aromatisation takes place intermolecularly, this being confirmed by a study of the reaction of *ortho*-tritiated benzylmagnesium chloride with formaldehyde[20]. The intermolecular mechanism of the aromatisation was proved[31]. in the reaction involving the protonation of and elimination of mercury from *ortho*-deuteriated benzylmercury chloride:

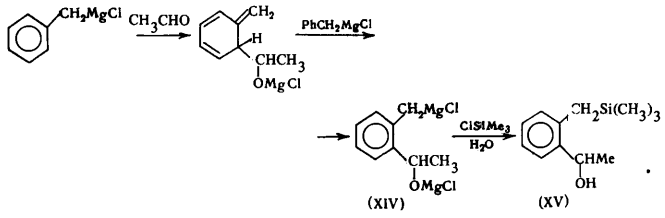


The lower deuterium content in toluene compared with the initial benzylmercury chloride is evidence of intermolecular aromatisation of compounds (XIIIa) and (XIIIb). The identical deuterium contents in toluene and in the benzoic acid obtained as a result of its oxidation suggest that the entire deuterium is located in the benzene ring, which could not occur in the intramolecular migration of the proton in compounds (XIIIa) and (XIIIb).

The intermolecular mechanism of the aromatisation of the methylenecyclohexadiene intermediates is also confirmed by the formation of deuteriated ethyltoluenes when the reaction mass obtained in the alkylation of benzylmagnesium chloride with diethyl sulphate is decomposed by deuterium chloride[37]:



It is also possible to postulate another pathway to the aromatisation of methylenecyclohexadiene compounds in this reaction: their interaction with an excess of the organometallic compound, the formation of a secondary organometallic derivative, and its reaction with deuterium chloride. However, not even traces of alkylation products of the secondary organomagnesium compounds could be detected in this case. The formation of the secondary organometallic product was demonstrated in another instance — in the interaction of benzylmagnesium chloride with acetaldehyde, which results in the formation of appreciable amounts of a diaddition product. The addition of the alkylating agent $ClSi(CH_3)_3$ to the reaction mixture yielded the alcohol (XV) — the alkylation product of the secondary organomagnesium compound (XIV):



Since the aromatisation of methylenecyclohexadiene compounds takes place via an intermolecular mechanism, it follows that the process (and hence the yield of the corresponding reaction products substituted in the aromatic ring) should depend on the nature of the neutralising agent. Experiments confirmed this conclusion[36]. Neutralisation of the reaction mass in the reaction of benzylmagnesium chloride with α-chloro-methyl ether by a strong acid (HCl) leads to higher yields of the "anomalous" products than neutralisation by a weaker acid (ammonium chloride). In the latter case there is apparently insufficient time for the dihydro-products to be aromatised and to undergo any changes (e.g. dimerisation[39]) in the course of subsequent isolation. On the other hand, the yield of the normal reaction product remains almost constant regardless of the agent employed.

The above mechanism covers also cases of *ortho*-substitution. There are no literature data on the basis of which a mechanism for *para*-substitution might be devised. One can suppose that, whereas *ortho*-substitution takes place via the interaction of one molecule of the nucleophilic agent with one molecule of an electrophilic agent, the *para*-substitution reaction requires the involvement of a larger number of molecules. One may point to the closely analogous instances where products of the 1, 2-, 1, 4-, and 1, 6-addition of a Grignard reagent to conjugated systems are formed[40, 41]. Whereas 1,2- and 1, 4-addition can be accounted for by a mechanism involv

the coordination of the metal to the carbonyl and the formation of a quasi-six-membered ring, the involvement of several molecules of the Grignard reagent is postulated to account for the 1,6-addition.

III. FACTORS INFLUENCING THE MODE OF REACTION

1. Electronic Structure of Arylmethylmetal Compounds

Examination of the mechanism of the reactions of arylmethylmetal compounds permits an approach to the consideration of the problem of factors affecting the mode of reaction. Although in the majority of studies on the chemistry of arylmethylmetal compounds, the influence of conditions on their reactivity has been demonstrated, there is no unanimous view in the literature on the causes responsible for changes in the mode of reaction. The number of studies specially undertaken on this question is small and the great sensitivity of the reaction to slight (at first sight) changes in conditions frequently makes it difficult to compare the results of different investigators. Comparable data have been taken as a rule from one investigation or from several investigations carried out under identical conditions.

We believe that it is valid to consider the reactions of arylmethylmetal compounds as process involving ambident anions. An ambident anion is one with two reaction centres combined into a single conjugated system. The factors responsible for the dual reactivity of ambident anions have been investigated and described in a series of reviews[42-44]. However, most studies dealt with the behaviour of ambident anions the reaction centres of which are of different chemical types. Usually one of these is a carbon atom and the other a heteroatom, or both centres are different heteroatoms. The negative charge is distributed between the two centres in such a way that most of it concentrated at the more electronegative atom; the second atom is as a rule more polarisable.

The benzyl anion and in general arylmethyl anions constitute a special case of ambident‡ anions of the allylic type. Its characteristic feature relative to other ambident anions (particularly relative to the phenoxide ion which has an isoelectronic structure) is that both nucleophilic centres are carbon atoms, although in different states of hybridisation. As in heteroambident anions, the negative charge is distributed between both centres. According to modern hypotheses, by virtue of the low amount of *s*-character of the hybridised orbital, the unsaturated sp^2-hybridised carbon atom is more electronegative than the saturated atom[45]. Therefore, to a close approximation, one may assume that the negative charge is largely concentrated on the carbon atoms of the aromatic ring. However, the formal sp^3-state of the methylene carbon atom in the benzyl anion does not of course correspond to its true state. The delocalisation of electrons in the carbon-metal bond should lead to partial rehybridisation of the α-carbon atom. In the limiting case, this atom should also be sp^2-hybridised and all the bonds should be equalised. The actual state of the α-carbon atom is intermediate and depends on the structure of the compound, the nature of the metal and the solvent, and other factors.

The question of the state of the methylene carbon atom in certain organolithium compounds of the arylmethyl series was investigated recently with the aid of ^{13}C NMR spectroscopy[46-48]. The ^{13}C chemical shift is an effective measure of the hybridisation and charge density. The average chemical shift of the sp^2-hybridised ^{13}C atom is 60 – 70 p.p.m. and that of the sp^3-hybridised ^{13}C atom is 160 – 170 p.p.m. For a given constant hybridisation of the carbon atom, the ^{13}C shift δ is proportional to the electronic density at the carbon atom, as can be seen from a comparison of the chemical shifts in methane and methyllithium or cyclopentadiene and cyclopentadienyl-lithium (Table 3)[46,49]. An increase of electron density in such cases leads to a shift of the signal towards a lower field. In contrast, on passing from arylmethyl hydrocarbons to their lithium derivatives, δ decreases, which can only be due to a change in the hybridisation of the α-carbon atom from sp^3 to sp^2. The data in Table 3 show that the hybridisation of the methylene carbon atom in the monophenylmethyl compound is closer to sp^3 than for the di- and tri-phenylmethyl compounds.

Table 3. Effect of the charge on the ^{13}C chemical shift.

Compound	δ $^{13}C(CS_2)$	$\Delta\delta$ ^{13}C	Compound	δ $^{13}C(CS_2)$	$\Delta\delta$ ^{13}C
CH_4	196		Ph_2CH_2	157	
MeLi	209	13	Ph_2CHLi	114	—43
C_5H_5	—4*		PhMe	172	
C_5H_5Li	26*	30	$PhCH_2Li$	163	—9
Ph_3CH	132				
Ph_3CLi	102	—30			

* Relative to benzene.

Table 4. Negative charge densities at different positions in the aromatic ring of arylmethylmetal compounds according to NMR spectroscopic data.

Compound	Charge density			References
	ortho-	*meta-*	*para-*	
Ph_3CLi	0.000	0.080	0.130	50
Ph_2CHLi	0.080	0.070	0.160	50
$Ph_2C(C_8H_7)Li$	0.041	0.079	0.162	54
$Ph_2C(C_8H_{11})Li$	0.040	0.077	0.158	51
$(Ph_2CCH_2)_2Li_2$	0.015	0.070	0.155	52
$(Ph_2CCH_2)_2Na_2$	0.000	0.060	0.145	52
$(Ph_2CCH_2)_2K_2$	0.020	0.065	0.155	52
$(MePhCCH_2)_2K_2$	0.205	0.120	0.295	52
$PhCH_2Li$	0.120	0.100	0.180	50
2-$PyCH_2Li$	0.160	0.150 (4.6)	0.220	53

The charges at different positions in the benzene ring arising as a result of the delocalisation of electrons of the C - M bond were found from the ^1H NMR spectra of the organometallic compound (Table 4). For certain compounds, the charges were also calculated by the LCAO-MO and SCF methods[50], the result of the calculation by the SCF method agreeing satisfactorily with the experimental data. The charges on the central carbon atom were not determined experimentally. Their calculation, based on the assumption that the charge of the anion is -1, is

‡ In fact the benzyl anion is not an ambident but a polydent species; however, for the sake of simplicity we shall regard it as an ambident anion with two nucleophilic centres — the methylene carbon atom and an aromatic carbon atom without distinguishing the *ortho-* and *para*-positions.

inaccurate because the total negative charge is not located on the organic part of the molecules owing to the interaction between the cation and the anion.

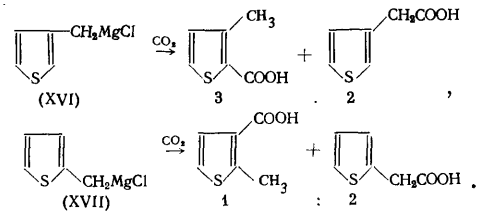
Although all the data quoted for the distribution of electron density in arylmethylmetal compounds refer to alkali metal derivatives, one may suppose that the situation is similar for other metal derivatives. Thus the spectrum of dibenzylmercury indicates the presence of fractional charges in the *ortho*- and *para*-positions in the benzene ring[55].

Thus the charge distribution in the molecules of arylmethylmetal compounds accounts for the attack of electrophilic agents both on the methylene carbon atom and on the aromatic part of the molecule. The mechanism of substitution in the aromatic ring discussed above in fact constitutes a special case of electrophilic substitution. It is evident that any factors promoting electrophilic substitution will increase the yield of ring-substituted products and will correspondingly diminished the yield of α-substituted products.

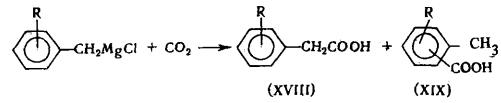
Experimental data show that an increase of electron density at any carbon atom of the aromatic ring facilitates the reaction at this centre of the ambident anion. Sherman and Anstutz[15] were already able to compare successfully various aryl residues in the reaction of arylmethylmagnesium chlorides with carbon dioxide. The yield of ring-substituted products increases in the series benzylmagnesium chloride < 2-thienylmethylmagnesium chloride < 2-furfurylmagnesium chloride. When electronegative groups are introduced into the aromatic ring, the conjugation between the C–M bond electrons and ring π electrons should increase with a corresponding increase of electron density at the carbon atoms of the aromatic ring, which facilitates the introduction of the electrophilic agent.

On passing from monocyclic compounds to their benzoderivatives, the yield of ring-substituted products increases. This was observed for the first time for heterocyclic compounds[19] and was then demonstrated in a comparison of benzyl and naphtylmethyl derivatives[23, 56]. Reactions of organometallic derivatives of 2-methylnaphthalene lead to 3-substituted and not 1-substituted derivatives, which may be related to a lower energy of charge localisation when the electrophilic agent attacks the 1-position[56, 57].

It is interesting to compare the two organometallic compounds (XVI) and (XVII). Owing to the $+I$-effect of the sulphur atom, substitution in the ring of the β-isomer (XVI) takes place to a greater extent than in the ring of the α-isomer (XVII)[58]:



It is evident that substituents in the benzene ring should have similar effect also on the dual reactivity of arylmethylmetal compounds. Since electron density in the *ortho*- and *para*-positions relative to the methylene group is important for the ring-substitution reaction, electron-donating groups in the *meta*-position should have the greatest effect. This has been confirmed by a study[59] of the carboxylation of various substituted benzylmagnesium chlorides:



A study of the effect of ring substituents on the kinetics of simultaneous deuteriation and demercuration of benzylmercury chloride provided convincing evidence for the effect of electron-donating *meta*-substituents[61, 62]. The products of this reaction contain considerable amounts of deuterium in the ring, which suggests a dual reactivity.

Table 5. Effect of the substituent in the benzene ring on the dual reactivity of benzylmagnesium chloride.

Compound	R	Yield, %	Compound	R	Yield, %
XVIII	H	100	XIX	H	0
	o-Me	100		*o*-Me	1
	p-Me	90		*p*-Me	10
	m-Me	30		*m*-Me	64*

* 2,4-dimethylbenzoic acid[60]

The proposed reaction mechanism involves attack by DCl on the ring *ortho*-position in the rate-limiting stage of the process (see Scheme 2). Data on the kinetics of the reaction of benzylmercury chloride and its methyl derivatives with deuterium chloride showed that the introduction of methyl groups in the *ortho*- and *para*-positions accelerates the reaction only slightly while a *meta*-methyl group has a significant influence on the rate. The effect of two *metal*-methyl groups is shown particularly clearly (Table 6).

Table 6. Relative rate constants for the simultaneous deuteriation and demercuration of substituted benzylmercury chlorides.

Ring substituent	K_{rel}	Ring substituent	K_{rel}	Ring substituent	K_{rel}
H	1	*p*-Me	2.11	2.6-Me_2	0.36
o-Me	2.44	*m*-Me	24.40	3.5-Me_2	$2.5 \cdot 10^3$

It is noteworthy that the results of such studies fail to reflect sufficiently clearly the effect of ring substituents on the dual reactivity of arylmethylmetal compounds, which is most probably due to incomplete isolation of all the reaction products[63–65].

2. The Nature of the Metal and Solvent

As already stated above, the mode of the reactions of arylmethylmetal compounds is influenced decisively by the hybridisation of the α-carbon atom. Delocalisation of the C – M bond electrons and hence rehybridisation of the

α-methylene carbon atom should depend on the nature of the metal. In the series of organometallic derivatives of magnesium, mercury, lithium, potassium, and caesium, an increase of the polarity of the C–M bond leads to a more intense conjugation of its σ electrons and the π-electron system of the ring. This change has been clearly demonstrated in a study[66] where the absorption spectra of various arylmethylmetal compounds were obtained (Table 7).

Table 7. Dependence of the absorption maximum of the benzyl compounds $C_6H_5CH_2X$ on the nature of the metal.

Substituent	λ_{max}	Substituent	λ_{max}	Substituent	λ_{max}
H	207	MgCl	266	Na	355
HgCl	245	Li	330	Cs	356

The shift of the absorption maximum of the principal band of the benzene chromophore when the substituent is altered arises from the change in the hybridisation of the α-carbon atom. When X = H, the methylene atom is in the state of sp^3-hybridisation — there is then minimal overlapping of the hybrid orbital with the π-electron system of the ring. The observed bathochromic shift of the absorption maximum in the spectra of organometallic compounds is associated with an increase of the overlapping of the valence electron orbital with the π-electron system of the aromatic ring. The increase is related to the change in the hybridisation of the α-carbon atom, the orbital of the valence electrons assuming an increasing p-character with increase of the amount of ionic character of the C – M bond. The maximum bathochromic shift in the case of ionic structures of sodium and caesium derivatives corresponds to the sp^2-hybridisation of the α-carbon atom. An analogous bathochromic shift with increasing electropositive properties of the metal has been observed in the absorption spectra of diphenylmethyl, triphenylmethyl, and fluorenyl anions[67, 68].

The change in the hybridisation of the methylene carbon atom as a function of the nature of the metal entails a change in its nucleophilicity and affects the reactivity of the organometallic compound as a whole. The closer the state of the α-carbon atom to sp^3-hybridisation the smaller the amount of ionic character of the C – M bond and the greater the degree of shielding of the α-carbon atom by the metal atom. This hinders the attack on the central carbon atom by the electrophilic agent and consequently leads to an increase of the relative reactivity of the aromatic carbon atoms. Conversely, when the α-carbon atom is sp^2-hybridised (maximum ionic character of the C – M bond), the central carbon atom is most accessible to interaction with the electrophilic agent. Despite the more marked conjugation of the C – M bond electrons with the aromatic ring π-electron system, in this case the aromatic carbon atoms are not as a rule attacked. Consequently dual reactivity should be shown to the greatest extent by derivatives of the most electronegative metals, for example Group III metals, and to the smallest extent by alkali metals.

Unfortunately a systematic comparison of the reactivities of arylmethyl derivatives of various metals has not been made under identical conditions, particularly due to the differences in the methods used to prepare the arylmethyl derivatives of different metals and their different solubilities. However, it is known that in the reactions of α-chloromethyl ether[36], dipropyl sulphate[37], and dicyanogen[57] carried out under comparable conditions with benzylmagnesium chloride and benzyl-lithium, dual reactivity is observed only for the magnesium derivative. The hypothesis of an appreciable dual reactivity of Group III metals has been confirmed by studies on tribenzylaluminium[69, 70] and tribenzylboron[11–13] published in recent years.

Together with these qualitative observations, individual quantitative data, listed in Table 8, have been published recently.

Table 8. Effect of the metal on the dual reactivity.

Nucleophilic agent	Electrophilic agent	Metal (electronegativity)	Ratio of yields of ring-substituted products and α-carbon addition products	References
$[Ph_2C{-}NPh]^{2-}2M^+$	iso-PrCl	K(0.91) Na(1.01) Li(0.97)	0.02 0.6 1.2	71, 72, 73
	iso-PrBr	K Na Li	0.1 1.0 3.0	71, 72
$\left[\begin{matrix}PhC{-}O\\ \vert\\ C_6H_{11}\end{matrix}\right]^{2-}2M^+$	CO_2	Na Li	1.7 2.4	74
$PhCH_2M$	$MeCH_2CHO$	Li $Mg_{1/2}$(1.23) $Al_{1/3}$(1.4)	0 0.4 5.0	75

The effect of the solvent on the reactivity of organometallic compounds is related primarily to the solvation of the cation and the state of the ion pairs in solution. The use of a polar (and particularly dipolar) solvent, which solvates effectively the metal cation, leads to an increase of the ionisation of the C – M bond, i.e. to an increase of the carbanionic properties of the compound. In other words, the solvent can influence the state of hybridisation of the α-carbon atom in the arylmethylmetal compound. This is confirmed by data for the dependence of the ^{13}C chemical shift in the NMR spectrum of $C_6H_5{}^{13}CH_2Li$ on the solvent (Table 9). (As already stated, the chemical shift reflects directly the state of hybridisation of the carbon atom.)

The data in Table[9] show that, with decrease of solvent polarity, the sp^3 character of the methylene carbon atom in benzyl-lithium increases.

The change in the state of hybridisation of the α-carbon atom naturally has an effect on the conjugation of the valence electrons of the C – M bond with the π-electron system of the ring. This is reflected in the absorption spectra of the organometallic compounds. Thus the main maximum in the absorption spectrum of 1, 1-diphenylhexyllithium undergoes a hypsochromic shift as the polarity of the solvent diminishes[76] (Table 10).

It is evident that the change in the state of hybridisation of the α-methylene carbon atom due to the change in the solvent or in the metal will have the same influence on

the reactivity of the compound as a whole. In a non-solvating (or in a weakly solvating) solvent, the state of the α-carbon atom approaches sp^3-hybridisation to the maximum extent, which hinders the reaction at this centre of the ambident anion. On the other hand, the use of a solvating solvent should promote the reaction at the α-carbon atom. The data in Table 11 show that a change in solvent polarity has a consistent influence on the proportions of the reaction products. It is important to emphasise that this relation has been found to hold for various reactions — alkylation, addition to the carbonyl group, and deuteriation. It is also significant that results in satisfactory agreement have been obtained for the same reaction by different workers. Admittedly, an unambiguous effect of the solvent is not observed in all cases.

Table 9. Effect of the solvent* on the ^{13}C chemical shift in benzyl-lithium[47, 48].

Solvent	$\delta^{13}C$	Solvent	$\delta^{13}C$
THF	163	Toluene	172
Ether	168.5	Benzene	174.5

* The following abbreviations are used in this and subsequent tables: THF = tetrahydrofuran; DME = 1,2-dimethoxyethane; TMED = tetramethylethylenediamine; HMP = hexamethylphosphoramide; DMF = dimethylformamide.

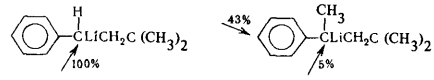
Table 10. Effect of the solvent on the absorption maximum of 1,1-diphenylhexyl-lithium.

Solvent	Dielectric constant	λ_{max}	Solvent	Dielectric constant	λ_{max}
THF	7.58	496	Propyl ether	3.88	422
DME	5.50	495	Benzene	2.28	426
Ethyl ether	4.33	438	Hexane	1.89	415

For example, the results obtained in the deuteriation of α-cumenylpotassium have not been explained, although replacement of ethyl ether by other solvents leads to the disappearance of dual reactivity regardless of solvent polarity. One must also point out the somewhat arbitrary nature of the table column labelled "solvent" — in many cases an excess of the given solvent was added to a solution of the organometallic compound in ethyl ether, so that the reaction actually took place in a mixture of the latter and the added solvent. This should not have an effect when a polar solvent, which effectively solvates the cation, is added, but becomes very significant following the addition of a solvent of low polarity. However, even with this stipulation, the principal feature, namely that a solvent solvating the cation facilitates the reaction with the α-carbon atom while a non-solvating solvent has the opposite effect, is evident.

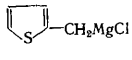
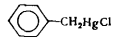
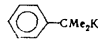
3. Steric Factors

Only isolated data have been published on the effect of steric factors on the dual reactivity of arylmethylmetal compounds. Thus the difference between the reactions of chlorodimethylsilane with the organolithium compounds (XX) and (XXI) has been explained by steric factors[79].



(XX) (XXI)

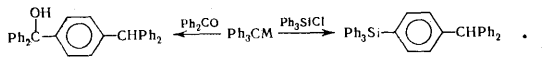
Table 11. Effect of the solvent on the dual reactivity.

Nucleophilic agent	Electrophilic agent	Solvent	Ratio of yields of ring-substitutes products and α-carbon addition products	References
	MeCOCl	Ether DME	0.5 0.5	58
	$ClCH_2OMe$	Ether THF	0.6 0.35	36
		Ether DME	0.14 0	37
	MeCHO	Ether THF	7 0.75	35, 75
	MeCHO	Ether DME THF TMED HMP	4 1.3 0.7 0.4 0.2	32
	$MeCH_2CHO$	Ether THF	0.3 0	75
	t-BuBr	n-Heptane Benzene Ether THF DME	3 2.7 0.07 0.01 0.01	77
	MeCOCl	Ether DME	19 0.9	58
	$CH_2—CH_2$ (O)	Ether DME	8 0	58
	DCl	Dioxan DME DMF	0.5 0.5 0.1	78
	DCl	Pentane Ether DME	0 0.3 0	3

Dual reactivity is shown by the organometallic compound (XXI), in which the carbon atom linked to the metal is tertiary. Similarly a change in reactivity is observed on passing from diphenylmethyl to triphenylmethyl derivatives of alkali metals. The reaction with ethyl benzoate[80], benzaldehyde, and benzophenone[81] results primarily in the formation of products of addition to the α-carbon atom, the secondary process yielding considerable amounts of products of *para*-substitution in the aromatic ring[82–84].

As already stated, derivatives of heavy alkali metals do not as a rule exhibit dual reactivity owing to their carbanionic properties. However, when cumenylpotassium is deuteriated[3], products resulting from attack on the ring are formed, which can probably be accounted for by steric

hindrance at the α-carbon atom. Steric factors have a particularly marked effect in those cases where both reactants (the nucleophilic and electrophilic agents) are sterically hindered. The interactions of alkali metal triphenylmethides with benzophenone[83] or chlorotriphenylsilane[4] can serve as examples:



The problem of the relation between the electronic and steric factors in reactions of dianions having the formula $Ar_2\bar{C}-\bar{X}$, where X = O or NC_6H_5, is somewhat more complicated. The presence of the second nucleophilic centre sharply increases the reactivity of the carbanion. Thus, in contrast to alkali metal diphenylmethides (XXII), which do not react with t-butyl chloride and acid nitriles in liquid ammonia[85,86], the dimetal derivatives of benzophenone (XXIII) interact with the above compounds under the same conditions[86,87]. The alkylation reaction proceeds not only with the α-carbon atom but also with ring carbon atoms. In the alkylation of these two compounds and also of compound (XXIV) with isopropyl bromide, the reaction proceeds in all cases, but compound (XXII) is alkylated only at the α-carbon atom, while (XXIII) and (XXIV) exhibit dual reactivity. The latter is probably due to the joint effect of both the electronic and steric factors:

$Ph_2CH^-M^+$ (XXII) $[Ph_2C-O]^{2-}\,2M^+$ (XXIII) $[Ph_2C-NPh]^{2-}\,2M^+$ (XXIV)

The study of the dual reactivity of the dianions $Ar_2\bar{C}-\bar{X}$ is complicated by two factors. Firstly, reactions involving the second anionic centre, for example *O*- or *N*-alkylation, are possible in addition to the dual mode of reaction of the ambident arylmethyl system. A reaction of the former type is observed in methylation but does not occur when more complex alkyls are employed[72,88]. Secondly, ring-substituted products can be formed not only as a result of electrophilic attack on the carbanion but also as a result of reactions by the intermediate radical-anion $Ar_2\dot{C}-X$. The formation of such radical-anions as a result of one-electron transfer in reactions of dianions has been postulated by a number of workers[72,89,90]. Radical-anions of the arylmethyl type are known to have a marked capacity for reactions involving ring carbon atoms (see, for example, Schenck and Matthias[91] and Holme and Crossland[92]).

4. Electronic Structure of the Electrophilic Agent

According to a familar rule, an increase of the positive charge on the electrophilic centre and also an increase of the polarity of the electrophilic agent should increase the tendency towards the reaction involving the atom of the ambident system which has the highest electron density. The numerous pieces of evidence supporting this hypothesis in relation to a series of ambident anions have been obtained as a rule in the alkylation reaction. In relation to arylmethyl anions, the reaction has been little studied, although there are isolated examples of a qualitative confirmation of the above rule in the case of alkylation[37]. The addition of the arylmethyl anion to the C = O bond (reactions with aldehydes, ketones, and acid derivatives) is more typical and better investigated. The electrophilic properties of carbon in these compounds increase in the series $CONR_2 < COOH < COOR < COR < COH < COCl$. The capacity of the reactants to form benzene ring-substituted products increases in the same sequence.

On the other hand, similar reactions have not been described for acids and amides, a few isolated observations have been made for esters, and aldehydes and acid chlorides are typical "anomalous" reactants. In a series of compounds of the same class, a change in the charge of the carbon atom due to the change in the properties of the aliphatic chain has a marked influence on the mode of reaction. Thus, whereas the reaction of benzylmagnesium chloride with acetonitrile results in the formation of the α-addition product only, the reaction with trifluoroacetonitrile yields up to 40% of the *ortho*-substituted products[7,8]. It has been shown[30,75] that in reactions of benzylmagnesium chloride with aldehydes, 100% substitution of the aromatic ring is observed only for formaldehyde, the yield of the ring-substituted product decreasing with increase in the length of the aliphatic chain. Branching at the α-atom, which reduces the charge of the carbonyl carbon atom§ has a particularly marked effect. On the other hand, when reactions of benzylmagnesium chloride with trifluoroacetaldehyde and acetaldehyde are compared, it is found that the ratio of the reaction product yields involving the ring and the α-carbon atom is greater by a factor of ten in the first reaction than in the second[35].

Table 12. Effect of reactant ratio on the yield of reaction products.

Nucleophilic agent	Electrophilic agent	Order of addition* and reactant ratio	Yield, %			References
			α-	*ortho*-	*para*-	
$PhCH_2MgCl$	PhCHO	Forward 1 : 1	90—84	0—2	—	84
		Reverse 1 : 1	43—40	20—60	—	93
$PhCH_2MgCl$	$ClCH_2OMe$	Forward 1 : 1	43	17	10	37
		Reverse 1 : 1	36	9	11	
$PhCH_2MgCl$	MeCHO	Forward 3 : 1	22	38 **	—	35
		Reverse 1 : 1	11—8	76—88 **	—	
α-$C_4H_4SCH_2MgCl$	$(CH_2)_2O$	Forward 1 : 1	45	53	2	58
		Reverse 1 : 1	25	72	3	
$[Ph_2C-NPh]^{2-}2Li^+$	iso-PrCl	Forward 1 : 1	46	45	9	72
		Reverse 1 : 2	34	57	9	

* The forward order of addition is understood as the addition of the electrophilic agent to the nucleophilic agent.
** The overall yield of the *ortho*-substituted product and the product of the simultaneous substitution in the *ortho*-position and at the α-carbon atom

An unusual example is provided by the deuteriation of cumenylpotassium[3]. Deuteriation of the ring, which takes place mainly in the *para*-position, depends on the polarity of the deuteriating agent. Whereas interaction with heavy water leads to selective α-deuteriation ($K_\alpha/K_{ring} > 500$), the ratio is 65 and 4.5 respectively in the reactions of CH_3COOD and with DCl.

There are also quite definite literature data concerning the effect of the ratio of the electrophilic and nucleophilic agents on the dual reactivity. Scheme 1 shows that the presence of an excess of the organometallic compound should favour the formation of products of the reaction

§ In this case, one cannot rule out also the effect of steric factors, as pointed out by Sadaaki and Yuya [spelling of names uncertain (Ed. of Translation)][75].

involving the α-carbon atom, while an excess of the electrophilic agent should promote ring substitution. This has been confirmed by experimental data (Table 12). It is interesting to note that the yield of *para*-substituted products is almost independent of the ratio of the reactants.

A brief examination of the mechanism of the "anomalous" reactions of arylmethyl compounds and the factors influencing these reactions leads to the conclusion that we now know the main general characteristics of this process. Moreover, in certain cases it is possible to alter the mode of reaction in order to obtain the desired result. However, our knowledge of the reactions of arylmethylmetal compounds requires further expansion. The question of the *para*-substituted products is least clear — even simple accumulation of experimental data on this problem is of definite interest and can lead to a hypothesis concerning the mechanism of *para*-substitution. On the other hand, the determination of the mechanism will ultimately make it possible to treat the arylmethyl anion not as an ambident species, which was done in the present review as a necessary simplification, but as a polydent anion, and to find conditions for reactions by such systems which are selective with respect to α-carbon atoms and the *ortho*- and *para*-carbon atoms in the ring.

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Radiation-chemical Processes in Radioactive Compounds

V.V.Gromov

Publications on the effect of the natural radiation of radioactive inorganic salts on their radiation-chemical stability are analysed. The main rules governing radiation-chemical processes in radioactive salts are examined. The effects of recoil atoms produced in radioactive disintegration, chemical impurities, and the intrinsic charge on the mechanism of the radiolysis of radioactive compounds are discussed. A detailed account is given of the effect of variation in the intensity of self-irradiation on the yield of decomposition products from certain radioactive salts (sulphates of Group II metals). A list of 55 references is included.

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I. INTRODUCTION

Within a few years of the discovery of radioactivity by Becquerel and the early papers of Mme Curie [1] radioactive isotopes were employed as indicators for the qualitative and quantitative determination of several elements, in studying the structure of chemical compounds, and also for observing the progress of processes involving substances containing a radioactive tracer. All such experiments were based on the assumption that the physicochemical properties of isotopes of the same element are identical, and that the effect of radiation from the radioactive isotope on the test materials could be neglected [2]. The first condition is satisfied if the difference in mass between the isotopes is relatively small: in practice it can be regarded as satisfied for elements of atomic number above ten [3]. The second condition by no means applies in all cases: very often radiation-chemical processes in the test systems have a significant influence on the physicochemical properties of radioactive compounds [4,5]. This applies especially to solid radioactive materials, in which disturbances due to the radiation may accumulate and remain for a long time.

With the development of atomic industry and the wider use of radioactive isotopes in science and various branches of the economy, it becomes increasingly necessary to study the properties of highly radioactive materials, which are subject to continuous self-irradiation. In atomic technology and in the preparation of labelled compounds, for example, materials must be handled whose specific radioactivity reaches several curies and tens of curies per gram. For practical purposes, therefore, it is extremely important to assess the effect of self-irradiation on various properties of highly radioactive materials, to determine their radiation stability.

Frequently these problems cannot be solved merely by investigating the effect of corresponding external irradiation on the systems. Even with bombarding particles of the same nature and energy there are definite differences between self-irradiation and external irradiation: (*a*) self-irradiation is continuous in time (as long as the radioactive isotope is present); (*b*) the dosage rate is usually low in self-irradiation; (*c*) the action of self-irradiation is usually uniform throughout a solid of any dimensions even with particles of low energy (provided, of course, that the radioactive isotope is uniformly distributed throughout the sample); (*d*) chemical impurities, which may be in various valency forms, are produced in the system by radioactive disintegration; and (*e*) recoil nuclei play a significant role in radioactive materials.

The above features of radioactive compounds demonstrate the need for a careful investigation of radiation-chemical processes occurring in radioactive salts. Unfortunately, not so many publications have yet appeared on this topic, and there have been no reviews of work that has been published. The present survey makes an attempt to fill this gap.

The chemistry of hot atoms (and also the self-radiolysis of organic compounds), which often exhibit problems similar to those of the radiation chemistry of solid radioactive compounds, will not be considered here. This field of research is of intrinsic value, and involves mainly the study of phenomena in neutron-irradiated materials, the measurement of the distribution of isotopes between individual chemical forms, and the separation of isotopes by means of the Szilard–Chalmers effect. Full information on these aspects can be found in several publications [3,6-9].

II. PRIMARY RADIATION PROCESSES IN RADIOACTIVE MATERIALS

The nature and the accumulation of the primary radiolysis products of crystalline radioactive compounds has been studied most fully on the radioactive sulphates of barium, strontium, calcium, magnesium, and potassium [10-16]. Isolated experiments have also been made on several carbonates [17-21], cobalt formate [22], and other compounds.

Self-irradiation even by low-energy β-particles may lead to considerable radiation-chemical changes. In the β-disintegration of tritium ($\overline{E} \simeq 6$ keV), for example, the bonds in the chemical compound containing $^3H_1$ may be ruptured [23]. If conditions are produced in a radioactive material such that radiation disturbances are not annealed, defects may gradually accumulate to considerable concentrations [24,25]. Thus 5 min after the start of an experiment, Lambe detected by electron spin resonance the accumulation of paramagnetic centres in mixtures of tritium and krypton frozen at 4.2° and 77°K. [26,27]

The introduction of α-emitters into crystals of complex salts produces more fundamental radiation-chemical changes than does the addition of β-radioactive isotopes.

Radiation disturbances (recorded by electron spin resonance) have been observed in $La_2Mg_3(NO_3)_{12}.24H_2O$ at room temperature immediately after the addition of americium-241 (3 mc g^{-1}).[28] Yet the β-radiation of promethium, present in this compound in similar amounts to americium (~ 3 mc g^{-1}), has such a weak effect that an e.s.r. signal appeared only three weeks after preparation of the salt. The radiation defects observed in this salt were attributed to NO_3, NO_2^-, and NO_3^{2-} radicals, which appear also after exposure of the salt to γ-quanta. Boyd and Ward showed[29] that the intensity of radiolysis of lithium bromate resulting from the fission of lithium-6 after capture of a neutron exceeds fivefold the intensity from the action of cobalt-60 γ-rays under similar conditions, the dose absorbed being $(1-40) \times 10^{22}$ eV $mole^{-1}$. The same products are formed in the two cases: i.e. the mechanism of radiolysis does not vary significantly with the method of irradiation. However, the experimental results are greatly affected by increase in the linear energy transfer on exposure to neutrons and subsequent fission of lithium-6. These processes are accompanied by a considerable rise in temperature in the tracks, which accelerates the radiation-thermal decomposition of lithium bromate.

Careful investigations on radioactive (sulphur-35) sulphates of barium, calcium, strontium[10-12], magnesium, and potassium[14-16,31,32] show that radiation defects of the same nature arise in radioactive and in inactive salts. In this respect the actions of external irradiation and of self-irradiation are equivalent. The radical-ions SO_4^- and SO_3^- are the chief primary products ("defects") in the above salts. Prolonged storage of the radioactive materials involves gradual formation of the ions SO_3^{2-} and SO_2^- and probably of SO_2.[16,32] At low temperatures an appreciable quantity of other, less stable radiation defects, whose nature has not been established, is also formed. The main features of the mechanism of radiolysis which applies to non-radioactive sulphates are preserved:

$$c \rightsquigarrow SO_4^{2-} \rightarrow SO_4^- + 2e\,(SO_3^-,\ O^-,\ e) \quad (1)$$

$$SO_4^- + e \rightarrow \overset{\bullet}{SO}{}_4^{2-} \begin{cases} \nearrow SO_4^{2-} + h\nu \\ \searrow SO_3^- + O^-\,(O + e) \end{cases} \quad (2)$$

$$SO_3^- + e \rightarrow \overset{\bullet}{SO}{}_3^{2-} \begin{cases} \nearrow SO_3^{2-} + h\nu \\ \searrow SO_2^- + O^-\,(O + e) \end{cases} \quad (3)$$

$$SO_3^- + SO_3^- \rightarrow SO_3^{2-} + SO_2 \quad (4)$$

The main difference between externally irradiated and radioactive salts lies in the variation in the concentration ratio of paramagnetic centres. Thus $SrSO_4^*$ of initial specific radioactivity ~ 100 mc g^{-1} gave the ratio $[SO_4^-]/[SO_3^-] = 16.5$ after 4 years (absorbed dose 2×10^{22} eV g^{-1}). In externally irradiated strontium sulphate (dose 5×10^{22} eV g^{-1}) this ratio is 0.5. Hence the main product in radioactive materials is the radical-ion SO_4^-, with very little formation of SO_3^- radicals. Yet the concentration of the latter radicals is increased appreciably by irradiation with fast electrons and γ-rays (comparable temperature conditions and doses). The probable explanation is that the mean energy of sulphur-35 β-particles (~ 55 keV) is approximately one-tenth of that of the Compton electrons from cobalt-60 γ-radiation (410 keV) and far smaller than the energy of the fast electrons. In the former case (or with an external source of low emitted energy), therefore, ionisation effects predominate with the formation of SO_4^- radical-ions in the crystals of the radioactive sulphates, but the probability of cleaving sulphur–oxygen bonds to form SO_3^- radical-ions increases, on γ-irradiation (cobalt-60) and exposure to fast electrons. This interpretation of the results requires further experimental verification.

The temperature of irradiation also affects the relative proportions of SO_4^- and SO_3^- radical-ions: in the main the former predominate at low temperatures, and the latter at room temperature. Hence rise in temperature accelerates the dissociation of excited sulphate ions by reactions (2).[31,32] This is consistent also with experimental results on the thermal stability of radical-ions in sulphates[31-33]: the most stable is SO_3^-, which, for example, is annealed in strontium sulphate only at $\sim 500^\circ$C; the radical-ion SO_4^- begins to disappear even at room temperature. Probably the interconversion and recombination of paramagnetic centres during the prolonged storage of radioactive salts even at room temperature also determine in considerable measure differences in the proportions of the radicals compared with externally irradiated specimens.

Variation in the ratio of primary and secondary products of radiolysis may depend not only on the duration of self-irradiation but also on the appearance of impurities and the influence of ionisation processes accompanying radioactive disintegration on the course of subsequent radiation-chemical changes. Thus in the β-disintegration of radioactive lanthanum-143 some 60% of the cerium atoms formed are in the quadrivalent state, and the remainder in the tervalent[34]. External irradiation by accelerated electrons does not produce such effects.

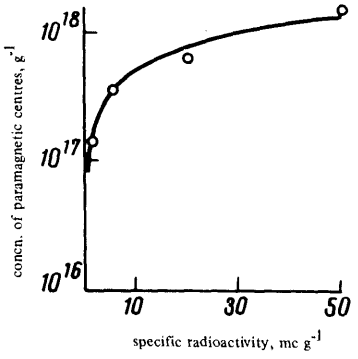


Figure 1. Dependence of concentration of paramagnetic particles on specific radioactivity of SrS^*O_4 at room temperature on keeping for 55 days.[11]

The radicals formed on exposure gradually accumulate to reach a limiting concentration[35-37]. This is a consequence either of kinetic effects directly in the irradiated zone or of afterprocesses in the thermodynamically non-equilibrium system. If the radicals are stable at room temperature (i.e. if they disappear slowly after exposure has ceased), it is easy to obtain curves representing the accumulation of paramagnetic centres. Fig. 1 shows the dependence of the total number of such centres on the specific radioactivity of strontium sulphate over the range 0.1–50 mc g^{-1}. In all cases the specimens were kept for 55 days, since the concentration of paramagnetic centres reaches its maximum value in this time. A similar variation is observed in all the radioactive sulphates investigated.

A characteristic feature of radioactive crystalline sulphates containing a "soft" β-emitter (sulphur-35) is that

the value of G_{pmc} in them is higher than in irradiated non-radioactive salts (Table), and the maximum concentration C^* of paramagnetic centres usually exceeds the corresponding values for externally irradiated materials (Fig. 2).

Parameters of the radiation stability of sulphates.

Sulphate	Crystal system	Radius of cation, Å	Ionicity of SO_4^{2-}	Lattice energy, kcal mole^{-1}	Free vol. of unit cell, Å^3	Self-irradiation at 25°C: initial specific radioactivity (^{35}S), mc g^{-1}	Self-irradiation at 25°C: G_{pmc}	External γ-irradiation at 30°C: G^*_{pmc}	External γ-irradiation at 30°C: $(SO_3^- + SO_2^-)$
$BaSO_4$	rhombic	1.43	0.46	589	88	20	0.7	0.5±0.18	(4±2.0)·10^{-2}
$SrSO_4$	rhombic	1.23	0.56	612	67	50	2.5	0.3±0.15	(2±0.7)·10^{-2}
$CaSO_4$	rhombic	1.09	0.71	647	76	50	—	(4±1.6)·10^{-2}	(7±3)·10^{-3}
$CaSO_4 \cdot 2H_2O$	mono-clinic	1.09	0.46	635	165	50	0.2	—	—
K_2SO_4	rhombic	1.32	0.5	432	136	—	—	5±1·10^{-3}**	1·10^{-4}

*G_{pmc} applies to the total paramagnetic centres formed on irradiation, but since $SO_4^- > SO_3^- + SO_2^-$ groups, it corresponds mainly to the primary products of radiolysis, which are SO_4^- radical-ions.
**Determinations made at −196°C.

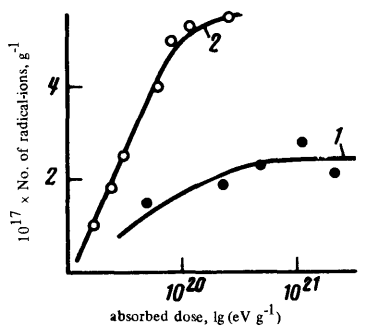


Figure 2. Accumulation of paramagnetic centres in barium sulphate at room temperature: 1) γ-irradiated salt; 2) radioactive BaS^*O_4 (20 mc g^{-1}).

Such relations between C_{irrad} and $C_{radioact}$ are characteristic of all the specimens studied, especially with small doses absorbed. This is probably because the radiation-chemical yield in radioactive salts corresponds to the number of paramagnetic centres in the zone of continuous irradiation. Hence, at any instant while self-irradiation is occurring, $C^*_{radioact}$ should exceed C_{irrad} by an amount corresponding to the number of paramagnetic centres that recombine rapidly after exposure has ceased (doses and dosage rates are assumed to be the same in comparable specimens). Experiment shows in fact that in radioactive sulphates $C^*_{radioact} \simeq (2-10)C_{irrad}$. Therefore the yields of paramagnetic centres are higher in radioactive salts than in externally irradiated specimens.

The appearance of a maximum in the time dependence of the concentration C of paramagnetic centres and the permanence of the relation $C^* > C_{irrad}$ can be explained [13] by an exponential decay in the intensity of self-irradiation with time, on the assumptions that radiation disturbances are reversible and are annealed both by direct recombination and under the influence of the emission itself (radiation anneal). The generation and destruction of radicals by a mechanism of "removal and addition" of electrons on exposure, which is characteristic e.g. of radioactive sulphates when the SO_4^- radical-ion is formed, satisfies these conditions. With the above limitations, and bearing in mind that [37,38] the annealing and production of defects have first-order kinetics, we obtain the formula [13]

$$\overset{*}{C}_t = a\exp\left[\frac{b}{\lambda}\exp(-\lambda t) - at\right]\int_0^t \exp\left[(\alpha-\lambda)t - \frac{b}{\lambda}\exp(-\lambda t)\right]dt \qquad (5)$$

where a, b, and α are coefficients depending on the probabilities of formation and disappearance of defects and on the initial intensity of irradiation, with $a > b$. Introduction of the dimensionless variable $\tau = \lambda t$ (in which λ is the disintegration constant and t the time), expansion of the integrand as a series, and integration yield

$$\overset{*}{C}_\tau = \exp(a e^{-\tau} - \sigma\tau)\sum_{n=0}^{\infty}\frac{(-\alpha)^n}{n!(n+\gamma)}\{1 - \exp[-(\alpha-\lambda)t]\} \qquad (6)$$

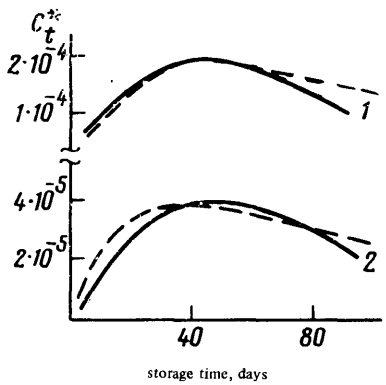


Figure 3. Variation in relative quantity of radicals in strontium and barium sulphates containing radioactive sulphur (20 mc g^{-1}):[13] 1) SrS^*O_4; 2) BaS^*O_4. Here C^*_t is the total number of paramagnetic centres divided by the number of irradiated molecules in 1 g.

Depending on the relation between the parameters α and σ the plots of the number of radiation defects C^*_T against the reduced time τ pass through a maximum, whose height and position are determined by the values of these constants.

Fig. 3 illustrates experimental and calculated ratios (to ±10%) of the number of radicals to the number of molecules irradiated in 1 g of BaS^*O_4 and SrS^*O_4. During storage of the radioactive material (the radioactive isotope disintegrates in conformity with the law $I = I_0\exp(-\lambda t)$,

where I is the emission intensity) a maximum occurs in C_t^*, and Eqn. (6) describes quite accurately the curves for the accumulation of radicals in radioactive materials. From the derivation of formulae (5) and (6) it follows that the maximum in the C_t^*–t curves is due to the fact that the spontaneous annealing of defects becomes of decisive importance with decrease in the emission intensity.

When the intensity of the emitter remains practically unchanged—i.e. $\lambda \simeq 0$ and $I = I_0 = \text{const}$—no maximum is observed. In this case the variation in Ct with time is represented by the formula

$$C_t = \bar{C}\{1 - \exp[-(b + \alpha)t]\}, \quad (7)$$

where the equilibrium concentration of defects is

$$\bar{C} = nAIP_1/(AP_1I + AP_2I + BP_3);$$

n is the number of irradiated molecules, P_1, P_2, and P_3 are the probabilities of the formation and disappearance of defects under the influence of irradiation and of their recombination, I is the dosage rate of the emission, and A and B are constants depending on the properties of the specimen and the conditions of irradiation.

Equations (6) and (7) show that an equilibrium number of defects may accumulate in the irradiated materials, their concentration at a given temperature depending solely on the properties of the medium and the intensity of self-irradiation[35,36,38].

It follows from Eqn. (7) that, with a constant intensity of irradiation, the number of radiation defects reaches $\bar{C}$ more rapidly the larger are P_1–P_3. Furthermore, Ct tends to $nP_1(P_1 + P_2)$ with increase in the dosage rate I (since $IAP_1 + IAP_2$ becomes $> BP_3$: i.e. spontaneous recombination of defects is small). Thus the equilibrium concentration of defects should be greater at higher values of I with the same dose absorbed. With decrease in the intensity of the emitter, Ct tends to $nIAP_1/BP_3$ (in this case $AP_1I + AP_2I > BP_3$). When $I = 0$, the formulae are devoid of physical meaning.

A possible reason why the number of radicals in materials containing radioactive isotopes is larger than in the externally irradiated non-radioactive compounds, under otherwise similar conditions[11–13], is that spontaneous annealing continues (rapidly at first, and then more slowly) after the termination of exposure, and by the time defects are recorded some of them have inevitably disappeared. Radioactive materials are under continuous irradiation, and therefore a higher concentration of defects is maintained in them. If the annealing of defects is negligible (e.g. at low temperatures), the same number of radiation disturbances accumulate in the two cases (external irradiation and self-irradiation). The formulae obtained for the accumulation of radiation defects in radioactive salts reflect only one aspect—the variation in the intensity of self-irradiation with time—of this complicated process. This effect is unable, of course, to explain all the features of radiation-chemical phenomena in radioactive crystals. As already mentioned, the accumulation of impurity atoms and specific aspects of the ionisation of electron shells in radioactive disintegration are of great significance here. Unfortunately, the influence of these factors has still not been adequately studied.

The above rules for the accumulation of paramagnetic centres apply only with identical or almost identical linear energy transfers in comparable specimens. Furthermore, if the transfer is large, a smaller quantity of disturbances may even accumulate in radioactive materials than in irradiated samples. In frozen water containing tritium (1 c ml^{-1}), for example, the yield of atomic hydrogen is about one-half of the yield in γ-irradiated ice with the same doses absorbed[24,25]. This is explained by intense recombination of radicals in the tracks. However, experiments with radioactive crystals of barium, strontium, and calcium sulphates revealed no variation in G(pmc) with the content of the radioactive isotope up to specific radioactivities of ~ 150 mc g^{-1}.

III. SELF-RADIOLYSIS OF RADIOACTIVE MATERIALS

Radioactive compounds may undergo considerable changes as a result of radiation-chemical processes. The radiolysis products gradually accumulate in them, and change the physicochemical properties of the radioactive specimens. Even the low-energy β-radiation emitted by carbon-14 affects the kinetics of the thermal decomposition of certain radioactive carbonates[17–21,39–41]. Thus the temperature of the vacuum decomposition (10^{-4}–10^{-5} mmHg) of CdC^*O_3 and $NaHC^*O_3$ of specific radioactivity up to 120 mc g^{-1} is about 60% [sic] lower than that of the non-radioactive salt. The form of the decomposition curves also changes: radioactive cadmium carbonate and radioactive sodium bicarbonate in a vacuum or in an atmosphere of nitrogen exhibit a maximum (sometimes even two maxima) on the rate curves (especially well defined with cadmium carbonate), whereas the non-radioactive salts show a minimum[40,41]. The composition of the gaseous products did not depend on the action of radiation.

These effects are explained[39] by increase in the reactivity of the radioactive carbonates due to the accumulation of radiation disturbances under the influence of the β-disintegration of carbon-14 (recoil atoms, the appearance of impurity centres—nitrogen atoms—rupture and distortion of chemical bonds, and the establishment of a local charge).

Cadmium carbonate was more sensitive to radiation than sodium bicarbonate. Thus CdC^*O_3 even of specific radioactivity 0.5 mc g^{-1} possesses enhanced reactivity, whereas $NaHC^*O_3$ of 95–120 mc g^{-1} (with respect to carbon-14) differs little in rate of thermal decomposition from the non-radioactive salt. Radioactive disintegration is assumed to facilitate the generation of a reaction centre but to have no appreciable effect on its migration inside the crystal. The second stage, almost unaffected by self-irradiation, is evidently the most important in the case of sodium bicarbonate. It is probable that not only different structure-sensitive properties of a solid but also various kinetic characteristics of a chemical reaction involving it will have different sensitivities to radioactive disintegration. This view is supported also by a kinetic investigation of the thermal decomposition of radioactive mercuric oxide (specific radioactivity (^{203}Hg) ~ 50 mc g^{-1}), whose kinetic parameters were identical with those of the non-radioactive analogue[42].

Detailed investigations have been made[43–47] of the spontaneous decomposition of plutonium and americium oxalates. At room temperature the simple and double oxalates of tervalent, quadrivalent, and sexivalent plutonium undergo vigorous decomposition with the evolution of gas under the influence of their own α-radiation[43–45]. After storage for 18 months the double ammonium, sodium, and potassium plutonium(IV) oxalates yielded a mixture of $PuOCO_3$ and $(Na, K)_2CO_3$. Pure plutonium(IV) oxalate gave a product corresponding in composition to plutonium oxide carbonate[44,45].

The decomposition of americium oxalate occurs so rapidly that the almost pure carbonate remains after

twenty days (Fig. 4). The efficiency of decomposition is 1.3 mol. per 100 eV of absorbed energy. The oxalate is converted into the carbonate, and carbon dioxide and monoxide are evolved. It is significant that the composition of the evolved gases and the final compound in the thermal decomposition of americium oxalate closely resemble the products of its radiolytic decomposition [46,48].

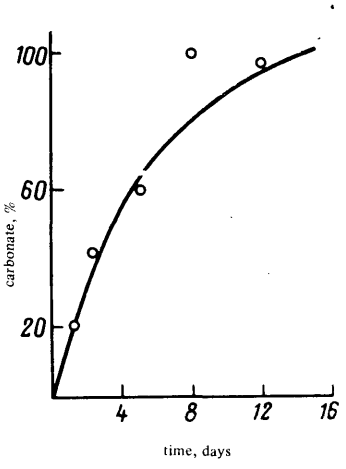


Figure 4. Variation with time in the carbonate content of americium oxalate crystals [47].

The addition of cobalt-60 to cobalt formate in amounts of 1.42 mc g^{-1} shortens the half-period of the topochemical decomposition of the radioactive salt to less than one-quarter. A gas comprising hydrogen and carbon dioxide is evolved. The effect of self-irradiation on the kinetics of the radiolysis of cobalt formate depends on the length of storage of the radioactive material, which involves the accumulation of radiation defects in the crystal lattice.

The contamination of silver azide with cadmium atoms by the disintegration of silver-110 (initial radioactivity ~ 3.5 mc g^{-1}) increases the detonation velocity of the azide by 50%. The accumulation of cadmium for 270 days changes the crystals from almost colourless to brown [49]. It is supposed that cadmium atoms and radiation defects (F-centres, displaced atoms) accelerated the decomposition of silver azide.

Insufficient data have been published on the self-radiolysis of radioactive materials for definite generalisations to be made. Barium, strontium, calcium, and potassium sulphates are exceptional in this respect.

An important parameter of the radiation properties of any system is the primary yield of products determined when the recombination of the disturbances can be neglected. Values of G_{pmc} for crystalline specimens are usually found from the initial linear portion of the curves representing the accumulation of paramagnetic centres at low temperatures. Values obtained with the irradiated salt at a high temperature, although different from the primary yields, can also characterise the radiation-chemical stability of solids (Table).

The Table shows that the yield of primary products of radiolysis of the sulphates, as well as of SO_3 groups + SO_2, which are formed mainly in secondary processes, decreases with increase in the lattice energy of the irradiated salts. Many workers have observed such a relation in series of compounds of the same type [50-52]. Hence the radiation stability of the crystalline anhydrous sulphates of the alkaline-earth metals conforms to the general rules of radiolysis established for other compounds. The ionicity† of the anion in the series of sulphates—barium, strontium, and calcium—has no appreciable effect on radiolysis (Table), the lattice energy being of decisive importance.

The radiolysis of radioactive sulphates under the influence of their own radiation supports the principle [51,53-55] that the radiation stability in the irradiated zone is greater in solids of smaller lattice energy: i.e. values of G_{decomp} are lower in crystals having smaller lattice energies (see "self-irradiation" column in Table). This is a characteristic feature of the self-radiolysis of radioactive salts, in addition to those noted previously—high values of G, rise in temperature, appearance of impurities and recoil atoms, and in some cases a maximum in the time dependence of the concentration of paramagnetic centres resulting from the exponential loss in intensity of self-irradiation.

The above experimental results are also a convincing demonstration that processes occurring in radioactive materials cannot always be simulated by external irradiation. The possible effects of self-irradiation must be thoroughly analysed in each specific case, and their role in the system carefully assessed.

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†The Russian text has "electronic fraction" (Ed. of Translation).

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Institute of Physical Chemistry,
USSR Academy of Sciences,
Moscow

U. D. C. 543.544

Present State of the Theory of the Chromatographic Microreactor

M.I.Yanovskii and A.D.Berman

Published information on the use of a pulse chromatographic microreactor in catalytic investigations is reviewed systematically. Theoretical analysis of the processes occurring in such a reactor showed the possibility of using transient pulse methods to determine the adsorption and desorption rate constants for starting materials and products during a catalytic process, to study the effect of longitudinal and internal diffusion, to reveal the principal and subsidiary paths of complicated catalytic processes, etc. From an analysis of published data it is concluded that chromatographic methods should be introduced more widely to solve complex kinetic problems in heterogeneous catalysis. A list of 90 references is included.

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I. INTRODUCTION

The invention in 1955 of the microcatalytic reactor, by Kokes et al. [1] just three years after Martin had formulated the principles of gas–liquid chromatography [2], advanced significantly the range of application of chromatography in catalysis. In essence the method is extremely simple: the reactor filled with the test catalyst is inserted into the gas circuit in front of the chromatographic column of an ordinary gas chromatograph. The microreactor is placed in a furnace to ensure a specified temperature in the catalyst bed, and a stream of an inert carrier gas is passed through continuously. A specified quantity of the reactant is periodically introduced as pulses into the microreactor. The reaction products and the unchanged material are carried into the chromatographic column by the stream of carrier gas.

Several modifications of the pulse method have now been described, but they all have the common features of rapidity, the possibility of using very small quantities of reactants and catalysts, and also great sensitivity [3].

Use of the microcatalytic reactor yielded within a short time voluminous and important information on both processes and catalysts for several important systems [4-6]. With highly sensitive detectors and efficient separating columns any side reaction, which might remain unnoticed in the usual method, could be recorded as well as the main reaction. In several cases we can begin to discern the chief features of the step-by-step mechanism of certain complicated reactions. It is already difficult to imagine a modern catalysis laboratory in which wide use would not be made of the microcatalytic reactor, together with the usual catalytic equipment, especially for the selection of new catalysts [7-10].

The present paper surveys the kinetics of catalytic reactions taking place in a microcatalytic reactor with the pulsed introduction of reactants. The kinetics of a process in a microcatalytic reactor may in general differ significantly from the kinetics in the flow-type and circulatory apparatus traditionally used for catalysis. We must distinguish several groups of factors responsible for these differences.

The first group depends on the difference in the state of the catalytic surface. In the microreactor the catalyst is continuously blown out at the reaction temperature by the stream of pure inert carrier gas.

Since a pulse usually introduces a very minute quantity of reactant into the microcatalytic reactor, results obtained for the first few pulses can often be regarded as representing the catalytic properties of a surface not yet subjected to the action of the reacting system. By introducing pulse after pulse or reactant into the microreactor, it is possible to trace a gradual change in catalytic activity during the catalytic process; this opens up the possibility of studying kinetics on catalysts operating under transient conditions. Belousov has paid close attention to this problem in a series of studies [11-13] of the mild oxidation of propene on a large number of oxide catalysts. When tested under steady-state conditions, the catalyst remains for a long time in contact with the reaction mixture, so that its surface is able to undergo significant changes. Many investigations have shown that the catalytic activity of a catalyst measured from the first few pulses in the microreactor sometimes exceeds by several powers of ten the activity determined under steady-state conditions.

The second group of factors responsible for the distinctive features of processes occurring in the microreactor depend on the movement of bands of starting materials and products along the catalyst layer, and also on the changes in the concentration profile and surface coverage resulting from diffusion, adsorption and desorption, etc. We shall examine below the effect of these processes on the kinetics of catalytic reactions in the microreactor.

II. IRREVERSIBLE REACTIONS

1. Reactions of Type A → B with a Linear Adsorption Isotherm for A, Rapid Establishment of Adsorption Equilibrium, and Absence of Diffusion Processes

An account of the theory of processes occurring in the microcatalytic reactor can easily begin with the simplest case, in which adsorption of the reactant A on the catalyst is rapid and is described by the linear Henry equation

$$a_A = \Gamma_A c_A \tag{1}$$

and the effect of diffusion on the blurring of the band can be neglected. Here c_A and a_A are the concentrations of A in gaseous and adsorption media respectively, while Γ_A is the Henry coefficient.

If we write the equation of continuity for flow of substance A across an elementary layer in the microcatalytic reactor, and take into account Eqn. (1) and the appropriate boundary conditions, we obtain a linear partial differential equation [14]. By solving this equation we can determine the concentration $c_A(x, t)$ of the reactant A in any cross-section x of the column at a specified time t:

$$c_A(x, t) = \psi(t - t_R)\exp(-t_R^{corr} k) \tag{2}$$

where $\psi(t)$ is a function describing the shape of the pulse fed to the microreactor, t is the time measured from the introduction of the pulse, t_R and t_R^{corr} are the usual parameters of a chromatographic experiment—the retention time and the "corrected" retention time [15] respectively—and k is the first-order rate constant of the heterogeneous catalytic reaction.

Equation (2) shows that the pulse of reactant A moves along the catalyst layer at a constant speed with a gradually diminishing height but without change in its original width. In this simple case the reaction rate constant can easily be determined by means of an equation analogous to the formula for a flow reactor:

$$k\Gamma = \frac{1}{\tau}\ln\frac{1}{1-\alpha} \tag{3}$$

where $\tau = v_{cat}/u_{vol}$, in which v_{cat} is the volume of catalyst in the microreactor and u_{vol} the space velocity of the carrier gas through the reactor; α is the degree of conversion, usually determined from the ratio of the peak area for A at the outlet from the microreactor to the corresponding area at the inlet.

For a first-order reaction α is independent of the distribution of the initial substance A along the reactor layer, i.e. on the form of the pulse. This enabled Habgood and Basset [16] to deduce Eqn. (3) without setting up differential equations relating the form of the pulse with time and position. This equation has been widely used to analyse experimental results obtained with the microcatalytic reactor [17,18]. Incidentally, experimental verification that α is independent of the form of the initial pulse for a first-order reaction has been reported in several papers [19,20].

Roginskii and Rozental' [21] examined the simultaneous occurrence of heterogeneous and homogeneous reactions in the microcatalytic reactor. Their solution was analogous to (2) with the constant k replaced by an effective constant

$$k_{eff} = \frac{(1-\varkappa)k\Gamma_A + \varkappa k^{hom}}{\varkappa + (1-\varkappa)\Gamma_A} \tag{4}$$

in which k and k^{hom} are the rate constants of heterogeneous and homogeneous reactions respectively, and $\varkappa$ is the free volume of the batch. The observed activation energy of the reaction E_{obs} can be determined from the temperature variation of k_{eff}. If only a heterogeneous reaction takes place in the reactor, we have

$$E_{obs} = E_{true} - Q_{ads} \tag{5}$$

When only a homogeneous reaction occurs, then

$$E_{obs} = E_{true} \tag{6}$$

Ample information on the kinetics of a reaction of type A → B in the microreactor can be obtained [22-25] from the form of the peak for product B recorded immediately beyond the microreactor. The form of this peak was described by solving the set of differential equations for the material balance of A and B with linear adsorption isotherms.

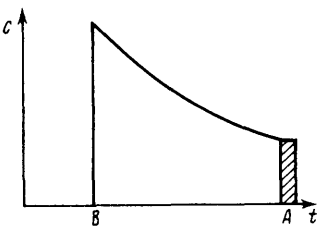


Figure 1. Diagram of chromatogram obtained directly after reactor, for the reaction A → B.

It was supposed [24,25] that a narrow band of the starting material A of width δ had been introduced into the originally empty microcatalytic reactor. The following picture of the movement of the bands of A and B along the catalyst bed emerges from these results. On the right of Fig. 1 is shown hatched the band of reactant A, which, without changing its initial width δ, moves at a speed inversely proportional to Γ_A, while gradually diminishing in height (e.g. Eqn. 2). The right-hand boundary of band B is adjacent to band A and moves at the same speed. The left-hand boundary of band B moves at a speed determined by the coefficient Γ_B. Thus the width of band B is governed by the difference $\Gamma_A - \Gamma_B$ and the form by the rate constant k. The retention time of band B can usefully be determined from the elution time of the centre of gravity of the band t_{cg}^B, for which the relation

$$t_{cg}^B = t_A^R + \frac{\Gamma_A - \Gamma_B}{\Gamma_A k} + \frac{t_A^R}{\alpha}\left[\frac{\Gamma_B}{\Gamma_A} - 1\right] \tag{7}$$

has been obtained [25]. For rapid reactions ($k \to \infty$, $\alpha \to 1$) it follows from (7) that

$$t_{cg}^B = t_A^R \frac{\Gamma_A}{\Gamma_B} \tag{8}$$

With small degrees of conversion

$$\alpha \approx 1 - \exp(-k t_R) \approx k t_R$$

we find that

$$t_{cg}^B \approx {}^1/_2 t_A^R \cdot \left(1 + \frac{\Gamma_B}{\Gamma_A}\right) \tag{9}$$

It has been shown also that the blurring of the band of products B is proportional to the square of the relative difference between the Henry coefficients for A and B, and depends also on k and α:

$$\sigma_B^2 = \left(\frac{\Gamma_A - \Gamma_B}{\Gamma_A}\right)^2 \left[\frac{1}{k^2} - \frac{t_A^R}{\alpha}\left(\frac{1}{\alpha} - 1\right)\right] \quad (10)$$

Formulae (7) and (10) can be used for the experimental determination of k and Γ_B.

Calculations have been made [22,23] of the form of the hydrogen band produced by dehydrogenation when a broad rectangular pulse of cyclohexane is admitted to a microreactor filled with a platinum–alumina catalyst. The microreactor was followed by a column containing activated carbon, which completely absorbed unchanged cyclohexane and the benzene formed, while hydrogen passed through. From the shape of the hydrogen band it was possible to calculate the reaction rate constant k and the activation energy for the dehydrogenation of cyclohexane to benzene.

2. Reaction of Type nA → B with a Linear Adsorption Isotherm for A and Rapid Establishment of Adsorption Equilibrium

The progress of an irreversible reaction of order n with a linear adsorption isotherm for the starting material A and rapid establishment of adsorption equilibrium has been considered in the paper cited above [14]. The equation of material balance together with the linear isotherm yields the solution

$$c_A(l, t) = \frac{\psi(t - t_{cg}^R)}{\sqrt[n-1]{1 + (n-1)\, k t_A^{coff} \Gamma_A^{n-1} \psi^{n-1}(t - t_R^A)}} \quad (11)$$

where $\psi(t)$ is the form of the entering pulse and l the length of the catalyst bed. The self-evident relation

$$1 - \alpha = \frac{\int_{t_A^R}^{T + t_A^R} c_A(l, t)\, dt}{\int_0^T \psi(t)\, dt} \quad (12)$$

exists between α and the size and shape of the pulse of A at the inlet to the microreactor. From Eqns. (11) and (12) expressions have been obtained [14] for calculating the constants k from definite experimental values of α with $n = 0$, 1, 2 for rectangular and triangular pulses.

It is possible to determine n and k by conducting the reaction at small values of α in the microreactor [28]. The rate w of a catalytic reaction in the microreactor can be written

$$w = \frac{\Delta m}{\Delta t \cdot v_{cat}} \quad (13)$$

where Δm is the quantity of material converted and Δt the residence time of the reactant band on the catalyst bed of volume v_{cat}. Although α depends on the form of the pulse when $n \neq 1$ the differences do not exceed 10–15% if pulses having the same mean concentration c_{av} are compared. The reaction velocity in the microreactor can therefore be related to the mean concentration in the pulse, and a correction then made for the shape of the latter:

$$w = \frac{\Delta m}{\Delta t \cdot v_{cat}} = k_{eff} \Gamma^n c_{av}^n \quad (14)$$

in which $k$eff is an effective rate constant based on c_{av}.

It follows from (14) that the order of the reaction is determined from the slope of the linear plot of $\lg w$ against $\lg c_{av}$, and $k$eff from the intercept made by this straight line on the vertical axis. To determine the true rate constant k we must introduce a correction for the form of the pulse:

$$k = k_{eff} \frac{\left[\frac{1}{T}\int_0^T \psi(t)\, dt\right]^n}{\frac{1}{T}\left[\int_0^T \psi^n(t)\, dt\right]} \quad (15)$$

This equation was obtained by expanding formula (11) for the elution curve as a Taylor series, and substituting the approximate value of $c_A(l, t)$ in (12). Germain [28] obtained an analogous expression by a somewhat different method.

When $n = 0$ or 1 the correction calculated from the ratio of integrals on the right-hand side of Eqn. (15) is unity: i.e. $k$eff $= k$ for reactions of zero and first order, independently of the form of the pulse. In the case of rectangular pulses this correction can be shown also to be unity for any value of n.

The above method has been used [29] to study the oxidative dehydrogenation of isopentenes to isoprene on a catalyst comprising a mixture of the oxides of iron, chromium, and zinc.

If the order of the reaction is determined from (14) and substituted in (11), the approximate formula

$$(1 - \alpha)^{1-n} = (n - 1)\, c_{av}^{n-1} k \Gamma^n \tau \quad (16)$$

can be obtained instead of the input function of the mean concentration c_{av} in the pulse. This gives another simple procedure for determining the apparent rate constant [27]. The slope of the dependence of $(1 - \alpha)^{1-n}$ on τ is $(n - 1)k\Gamma_A^n c_{av}^{n-1}$. Determining c_{av} from the form of the pulse at the inlet to the microreactor, we can calculate the approximate value of $k\Gamma_A^n$ by dividing the slope by $(n - 1)c_{av}^{n-1}$.

3. Effect of Diffusion on an nth-Order Reaction of Type nA → B

An examination has been made [30] of the kinetics of nth-order reactions with longitudinal diffusion and rapid establishment of adsorption equilibrium. Since the diffusion equations are non-linear in this case, a mathematical solution cannot be obtained. We therefore assumed that the reaction had no significant effect on the blurring of the band of the initial substance. This can be expressed mathematically by writing

$$c_A(x, t) = c_A^0(x, t)\, N(t)$$

where $c^0(x, t)$ is the solution of the corresponding problem for gas-adsorption chromatography in the absence of reaction, and $N(t)$ is a function of time. If the relation

$$\frac{dc_A}{dt} = k\Gamma^n c_A^n(x, t),$$

is satisfied at every point in the bed, integration with respect to x and substitution of the preceding expression for $c_A(x, t)$ yields for $N(t)$ an ordinary differential equation, whose solution presents no difficulty. This is fully analogous to the approach used by Frank-Kamenetskii [31].

To summarise the principal qualitative results[30], diffusion has hardly any effect on the degree of conversion in first-order reactions ($n = 1$). Longitudinal diffusion slows down the reaction more strongly the higher the order of the reaction above unity. With second-order reactions the rate decreases in proportion to the square root of the time, owing to the diminution in the concentration in the reaction zone caused by blurring of the band. This effect becomes greater with increase in the length of the reactor bed and decrease in the rate of flow.

4. Reaction of Type A → B with Slow Establishment of Adsorption Equilibrium

In order to discuss the progress of a first-order reaction in a microcatalytic reactor taking into account the kinetics of adsorption[21] the usual material balance equation was solved together with the differential equation of sorption kinetics

$$\frac{\partial a_A}{\partial t} = k_A^a c_A - (k + k_A^d) a_A \qquad (17)$$

in which k_A^a and k_A^d are the rate constants of the adsorption and the desorption of substance A. An expression was obtained[21] for the form of the elution curve of A which included Bessel functions.

In the Reviewers' opinion it is more convenient, in the experimental determination of the rate constants k, k_A^a, and k_A^d, to use the expressions for the main parameters of the peaks of starting materials and products that can be obtained by the statistical method of moments[32]:

$$1 - \alpha = \exp\left\{-\frac{x}{u}\left[\frac{(1-\varkappa)k_A^a k}{(k+k_A^d)}\right]\right\} \qquad (18)$$

$$t_A^R = \frac{x}{u}\left[\varkappa + \frac{(1-\varkappa)k_A^a k_A^d}{(k+k_A^d)^2}\right] \qquad (19)$$

$$\sigma_A^2 = \frac{2x}{u}\frac{(1-\varkappa)k_A^a k_A^d}{(k+k_A^d)^3} \qquad (20)$$

where u is the linear rate of flow and σ_A^2 is the dispersion of the concentration distribution at the exit from the reactor.

With regard to the physical significance of the results, if the reaction occurs in the kinetic range ($k \ll k_A^d$), Eqn. (18) passes into Basset's well known equation (3). Thus Eqn. (3) applies (as is usually supposed) not only when adsorption equilibrium is established instantaneously but also in the more general kinetic case with $k \ll k_A^d$. With this last condition it follows from Eqns. (19) and (20) that even the occurrence of a heterogeneous reaction has no effect on the retention time or the blurring of the reactant A band. If k and k_A^d are comparable, the occurrence of a reaction accelerates movement of the A band and diminishes blurring. When desorption is the limiting stage ($k \gg k_A^d$), the corrected retention time $t_A^{R\,corr}$ is inversely proportional to k^2, while σ_A^2 is inversely proportional to k^3.

If it is assumed that the initial substance A and the product B are sorbed independently, and that the adsorption of both substances conforms to a linear kinetic equation, it appears possible to study the kinetics of the catalytic reaction from the form of the B band. In this case[25] the set of equations for A must be supplemented by the material balance equation and the linear kinetic equation describing the movement of the B band. This set of equations has recently been solved by an operational method[25], to yield expressions for the retention time t_B and the dispersion of the band σ_B^2 of product B analogous to those obtained for A (Eqns. 18–20). Thus the retention time is

$$t_B = t_A + \frac{x(1-\varkappa)}{\alpha u}[\Gamma_B - \Gamma_A^{eff}] - \frac{k_B^a(k+k_A^d) - k_A^a(k+k_B^d)}{k \cdot k_B^d \cdot k_A^a} \qquad (21)$$

where $\Gamma_A = k_A^a k_A^d/(k + k_A^d)^2$ is the effective Henry coefficient for the starting material. It follows from (21) that the elution time of the reaction product should differ from its retention time in gas-adsorption chromatography, as has been confirmed experimentally[25]. In a study of the cracking of cumene on an aluminosilicate catalyst, a mixture of benzene and cumene was introduced into the reactor. The chromatogram obtained immediately following the reactor shows (Fig. 2) separate peaks for benzene added to the reactor and for benzene produced in the reaction.

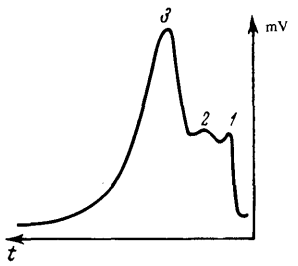


Figure 2. Chromatogram obtained after the microcatalytic reactor for the cracking of cumene on an aluminosilicate catalyst. A mixture of benzene and cumene was introduced into the reactor: 1) benzene added to the reactor; 2) benzene produced by the cracking of cumene; 3) cumene.

When $\Gamma_B = \Gamma_A^{eff}$, i.e. when the adsorption coefficients of starting material and product coincide, it follows from (21) that

$$t_B = t_A + \frac{1}{k_B^d} + \frac{1}{k + k_A^d} \qquad (22)$$

Thus even when $\Gamma_B = \Gamma_A^{eff}$ the peak of the product lags behind the peak of the initial substance a constant distance depending on the rate constant of the heterogeneous reaction and the desorption rate constants of starting material and reaction product.

An experimental method was also proposed[25] for studying the kinetics of adsorption during a catalytic reaction, involving the use of Eqns. (18)–(21) and corresponding expressions for complicated cases. The main difficulty to be overcome was that in this case the characteristics of the peaks due to individual substances at the outlet from the reactor were required for the calculation. Under normal conditions the separation of the components on the catalyst bed is seldom sufficient for direct measurements to be made. It was therefore suggested that the additivity

relations applicable to the reactor–column system[3] should be used:

$$t_c^R = t_p^R + t_\kappa^R$$
$$\sigma_s^2 = \sigma_r^2 + \sigma_{col}^2 \qquad (23)$$

where t_S^R and σ_S^2 are the retention time and the dispersion of the peak of a substance which has passed successively through the reactor and the column, t_r^R, σ_r^2 are the retention time and the dispersion of the peak of the substance after passing through the reactor, and t_{col}^R and σ_{col}^2 are the corresponding parameters for the peak after the substance has passed through the column.

The parameters t_S^R and σ_S^2 were determined from chromatograms at the outlet from the separation system, and t_{col}^R and σ_{col}^2 in a separate series of experiments in which a certain quantity of starting materials or products was introduced directly into the separating column. After this t_r^R and σ_r^2 were determined by means of Eqns. (23). This method was used to calculate the adsorption and desorption rate constants for cumene during cracking on an aluminosilicate catalyst.

5. Reactions of Type A → B in the Internal-diffusion Range

The method of moments was used by Rozental'[33] to analyse a complex case of movement of the band of substance A along the bed of the microcatalytic reactor, accompanied by a first-order reaction occurring in the inner-diffusion range. The analysis took into account also the kinetics of the adsorption of A on the internal surface of the catalyst. Effects of longitudinal diffusion were neglected. A set of three equations—(1) the kinetics of adsorption and the first-order reaction, (2) diffusion into the pores, and (3) material balance in the space between catalysts particles—was solved for this model. Application of the Laplace transformation to these equations yielded expressions for α, t_A^R, and σ_A^2 in terms of certain functions $f_0(z)$, $f_1(z)$, and $f_2(z)$ of the dimensionless variable $z = k\Gamma R^2/D_i$, in which R is the particle size of the catalyst and D_i the coefficient of internal diffusion.

The dimensionless parameter z defines the combined effects of adsorption, internal diffusion, and reaction on the form of the elution curve, while $f_0(z)$, $f_1(z)$, and $f_2(z)$ represent the effects of variation in α, t_A^R, and σ_A^2 as a result of diffusion in the pores during the reaction. Each of these functions decreases simultaneously with z and becomes unity when $z = 0$. This case corresponds to the absence of reaction or to rapid internal diffusion.

The function $f_0(z)$ is termed the fractional accessible surface[33]. It increases with decrease in Γ, k, and R; and decreases with decrease in D_i. Increase in $f_0(z)$ is accompanied by increase in α.

The quantity $\Gamma f_1(z)$ constitutes an effective adsorption coefficient. Diffusion combined with reaction diminishes the elution time of the peak of A. The contribution to dispersion due to the slowness of adsorption was also examined[33]. The occurrence of reaction was found to diminish the blurring due to diffusion into the pores.

6. Reactions of Type A → B allowing for Longitudinal Diffusion and Sorption Kinetics

The combined effect of adsorption kinetics and longitudinal diffusion on an irreversible first-order reaction has been examined by Kočirik[34]. The equations for the material balance and the adsorption kinetics of A are written

$$\varkappa \frac{\partial c_A}{\partial t} + (1-\varkappa)\frac{\partial a_A}{\partial t} + u\frac{\partial c_A}{\partial x} + k(1-\varkappa)a_A = D\frac{\partial^2 c}{\partial x^2}$$
$$\frac{\partial a_A}{\partial t} = k_A^a c_A - (k_A^d + k)a_A$$

where D is the coefficient of longitudinal diffusion.

The expressions for α and t_A^R obtained by the method of moments are

$$\alpha = 1 - \exp\left[\frac{u}{2D} - \frac{u}{2D}\sqrt{1 + \frac{4D(1-\varkappa)k\cdot k_A^d}{u^2(k+k_A^d)}}\right] \quad (a)$$
$$t_A^R = \frac{x}{u}\left[\varkappa + \frac{(1-\varkappa)k_A^a \cdot k_A^d}{(k+k_A^d)^2}\right]\frac{1}{r} \quad (b) \qquad (24)$$

where r denotes the square-root term in (24a). If the longitudinal diffusion coefficient D is small, Eqn. (24a) passes into (18). In general, however, diffusion combined with reaction accelerates the movement of A. Since r contains u^2 in the denominator, the effect of diffusion will be appreciable at low rates of flow.

An expression was also obtained[34] for the blurring of the band of A. In order to determine r and D experiments must be made at low rates of flow u; then k_A^a and k_A^d can be calculated from experimental results at high rates of flow.

7. Plate Theory of Heterogeneous Catalytic Processes in a Microreactor

The above discussion shows that considerable mathematical difficulties are involved in allowing for the simultaneous effects of adsorption kinetics and internal and external diffusion on retention times and dispersions. Several investigators have therefore tried to approach a solution to this problem on the basis of the "plate theory" employed in chromatography, which makes it possible to establish the effects of experimental parameters on the blurring of bands, although it will not reveal the mechanism of all the processes occurring in a column.

Kallen and Heilbronner[35] were the first to use the plate theory to analyse a process occurring in a microcatalytic reactor. On the assumption that the reaction A → B took place on every plate, differential equations were written for the material balance with respect to A and B. After solution by means of Laplace transformations, these yielded the following expression for the retention volume of A

$$v_{A\ reactn}^{R\ corr} = \frac{v_A^{R\ corr}}{1 + \frac{k v_A^{equiv}}{u_{vol.}}} \qquad (25)$$

Here $v^{R\,corr}$ is the corrected retention volume of A in the absence of reaction, and v_A^{equiv} the volume of developer necessary for the complete transfer of A from the nth to the $(n+1)$th plate.

Formula (25) is a qualitative indication of the same relations as obtained in preceding subsections, which allowed for adsorption kinetics and diffusion in analysing the process occurring in the microcatalytic reactor. In fact it follows from (25) that the reactant A moves more rapidly than in the absence of reaction, which is consistent with conclusions reached earlier for non-equilibrium

adsorption. The change in retention volume due to the reaction increases with increase in k. The retention volume decreases also with increase in v_A^{equiv}, i.e. with increase in the time required for the establishment of adsorption equilibrium.

The effect of reaction on the width b_A of the reactant A can also be assessed. On the basis of chromatographic theory[35] the width is determined by means of the relation

$$b_A = \frac{4\, v_A^R}{\sqrt{N}} \tag{26}$$

where N is the number of plates. According to (25) we have $v_A^{R\,reactn} < v_A^R$; therefore the width of the peak of reactant A is less than the width in the absence of reaction.

The equation

$$k = \frac{N\,(1-\sqrt[N]{1-\alpha})}{v_A^{R\,reactn}}\, u_{vol} \tag{27}$$

has been obtained to calculate k from data at different rates of flow of the carrier gas. Thus by determining α, $v_A^{R\,reactn}$, and N for different rates of flow it is possible to calculate the reaction rate constant.

Nakagaki and Nishino[36] calculated k for the catalytic isomerisation of cyclopropane into propene on a 13X molecular sieve, some of whose cations had been replaced by Ni^{2+}, using the catalytic chromatogram given by Basset and Habgood[16]. The equations for the profile of bands A and B obtained by means of the plate theory enabled several relations for the main characteristics of the peaks to be calculated[36] from the extent of reaction; these were qualitatively consistent with results obtained previously including kinetics and diffusion when analysing processes occurring in the microcatalytic reactor.

III. REVERSIBLE REACTIONS OF TYPE A ⇌ B

Two different approaches have been made to a theoretical analysis of reversible first-order reactions occurring in a microcatalytic reactor: in some papers the equations of material balance and kinetics have been solved; others have given a statistical treatment of the phenomenon, based on a probability study of the behaviour of molecules.

The reaction

$$A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B$$

has been examined[37] with instantaneous establishment of adsorption equilibrium and absence of diffusion complications. The statistical theory developed enables the concentration profile of A and B inside the microcatalytic reactor to be calculated for various series of parameters. The analyses show that, if a mixture of A and B is introduced into the microreactor, a broad band is formed initially, with peaks at the edges corresponding to A and B individually. After some time the band deforms into a single narrower peak containing both A and B in the equilibrium concentrations.

Klinkenberg[38] considered the occurrence of reversible reactions in a microreactor from a rather different point of view. In the case of linear adsorption, with instantaneous establishment of adsorption equilibrium and absence of diffusion complications, the material balance equation is written

$$u\frac{\partial c_A}{\partial x} + \varkappa\frac{\partial c_A}{\partial t} + (1-\varkappa)\frac{\partial a_A}{\partial t} = k_2 a_B - k_1 a_A = \left[u\frac{\partial c_B}{\partial x} + \varkappa\frac{\partial c_B}{\partial t} + (1-\varkappa)\frac{\partial a_B}{\partial t}\right] \tag{28}$$

Comparison of the result obtained by Klinkenberg on solving (28) with the result from Giddings' statistical method shows the same qualitative pattern. When a mixture of molecules of A and B is introduced into the microreactor, the peaks due to these components should disappear as equilibrium is approached, while an intermediate band containing molecules of A and B in equilibrium concentrations will steadily contract, approaching the width of the equilibrium band. The retention time of the equilibrium mixture is written

$$t_{AB}^{R\,eq} = \frac{x}{u}\,\frac{\frac{k_1}{\Gamma_B}[\varkappa + (1-\varkappa)\Gamma_B] + \frac{k_2}{\Gamma_A}[\varkappa + (1-\varkappa)\Gamma_A]}{\frac{k_1}{\Gamma_B} + \frac{k_2}{\Gamma_A}} \tag{29}$$

If a mixture of equilibrium composition is introduced into the microreactor, it will move at a mean speed, and emerge as a single peak after time $t_{AB}^{R\,eq}$. Thus, when for any reason it is important to avoid the occurrence of a reversible reaction in an analytical chromatographic column, a kind of "chromatographic azeotropy" will be observed, such that A and B will not be separated under the given conditions despite significant differences in Γ_A and Γ_B.

IV. THEORY OF REACTIONS UNDER CHROMATOGRAPHIC CONDITIONS

The separation of products and starting materials on the bed of the microreactor has a considerable effect on the course of the catalytic process. We shall show below, for example, that with reversible reactions the spatial separation of products or reactants has a significant effect on the degree of conversion by completely or partly suppressing the reverse reactions. In the case of consecutive reactions the separation of substances on the catalyst bed sometimes changes fundamentally the selectivity of the process.

The action of poisons will also be different under conditions of separation. Because of the difference in adsorption coefficients between poison and reactant, the poison band may not enter the reaction zone at all, and therefore not poison the catalytic process. Similar phenomena will sometimes be observed in the self-poisoning of the reaction by the products.

Finally we note that, with non-first-order reactions, the kinetics of the catalytic process is influenced also by the form of the concentration profile in the reaction zone, governed, as noted above, by the kinetics of adsorption and desorption, external and internal diffusion, etc.

The above features led us to combine in the same section cases in which the yield or the selectivity of the reaction is influenced by various chromatographic effects. Such reaction conditions in the microcatalytic reaction have been termed[39] "chromatographic". Theory shows[37] that the character of a chromatographic process is determined by the method used to move the chromatographic band along the layer of stationary phase. A chromatographic régime can therefore be established in various specific forms. We shall consider below mainly the elution

type of chromatographic process, which has recently been subjected to the most thorough theoretical analysis. However, this by no means exhausts the possibilities of the method.

1. Reaction of Type A ⇌ B + C

The equations describing processes occurring in the microcatalytic reactor with such reactions are non-linear. For the sake of simplicity, therefore, we shall consider only the case of a linear adsorption isotherm and instantaneous establishment of adsorption equilibrium. Let us examine first some general considerations[39].

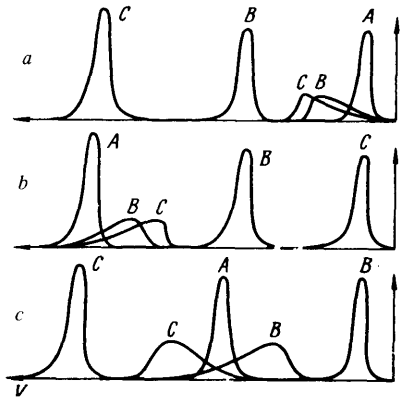


Figure 3. Diagram illustrating the establishment of a chromatographic régime.

Fig. 3 illustrates three possible relative arrangements of the A, B, and C bands on the catalyst bed, corresponding to the three relations among the adsorption coefficients —(*a*) $\Gamma_C > \Gamma_B > \Gamma_A$, (*b*) $\Gamma_A > \Gamma_B > \Gamma_C$, and (*c*) $\Gamma_C > \Gamma_A > \Gamma_B$. In case (*c*) (Fig. 3) the introduction of a narrow band of A should lead almost to cessation of reaction from right to left. In cases (*a*) and (*b*) the reverse reaction will be more strongly inhibited the larger the absolute difference $\Gamma_B - \Gamma_C$. This possibility of carrying out reversible reactions in one direction under chromatographic conditions was pointed out in Ref. 39, and has since been confirmed experimentally[40,41].

Magee[42] considered a reaction of type A ⇌ B + C under conditions such that its progress was limited solely by the equilibrium constant $K = c_B c_C / c_A$. He wrote down the equation of material balance, and solved it for the appropriate equilibrium condition by means of an analogue computer. He showed that with $K = 10^{-7}$ the reaction may be complete in a column 1 m long after only 17 s. It must be stressed that such large chromatographic effects, even with such small equilibrium constants, are due to the ideal character of the model, which disregards kinetic and diffusion effects. The displacement of equilibrium actually observed will always be smaller than the calculated shift.

To allow for the kinetics of a heterogeneous process with the present type of reaction under chromatographic conditions in a pulse microcatalytic reactor[27] the calculations are simplified by supposing that $\Gamma_A = \Gamma_C \neq \Gamma_B$.

Fig. 4 shows the dependence of α on the length of the layer calculated on an electronic computer. It is evident that α is significantly greater under chromatographic conditions than under dynamic conditions, but rather lower than for an irreversible reaction.

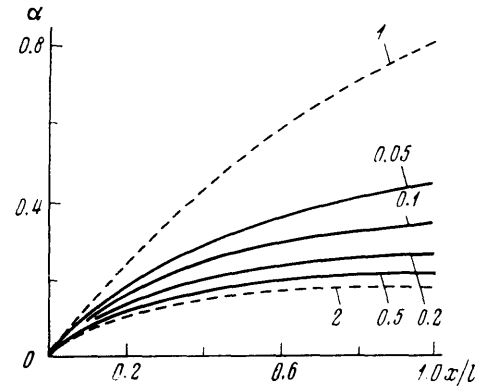


Figure 4. Dependence of degree of conversion α on dimensionless length x/l of catalyst bed for reaction of type A ⇌ B + C occurring under chromatographic conditions for different pulse widths τ_0 (numerals on full curves): 1) irreversible reaction; 2) flow-type reactor.

Hitherto we have been considering a single introduction of A into the microcatalytic reactor. However, if an attempt is made in the future to exploit in some measure the above chromatographic effects to develop a new technical process, the question should, of course, be raised of the possibility of introducing many such pulses into the reactor and of the interaction on the catalyst bed between bands from different pulses. Roginskii and Rozental'[43] tried to assess these effects by using an electronic computer to obtain calculated curves showing the dependence of α on length of bed for different durations of pulse and different intervals between their introduction. In all cases in such a cyclic process α reaches a maximum value in a reactor having an optimum bed length l_{opt}. The yield of reaction products could be increased by the chromatographic effects with a specified supply of starting material to the dynamic reactor and to the microcatalytic reactor.

When calculated values are compared with experimental results it must be borne in mind, however, that the kinetics of adsorption and diffusion were neglected in the above theoretical analysis of reactions of type A ⇌ B + C. In several cases these effects may be significant.

The reality of the chromatographic effects has been confirmed in several investigations. In a typical chromatogram (Fig. 5) obtained directly after the microreactor for the dehydrogenation of cyclohexane $C_6H_{12} \rightleftharpoons C_6H_6 + 3H_2$ on a platinum–alumina catalyst[40,44] the peaks due to cyclohexane and to benzene are clearly separated. Since an argon ionisation detector[3], was used, which was very insensitive to molecular hydrogen, the latter was not detected on the chromatogram. Comparison of the curves for the dehydrogenation of cyclohexane under

chromatographic conditions with the equilibrium curve and with the curve obtained in a dynamic reactor showed that chromatographic conditions raised the yield of benzene significantly above the equilibrium value. Matsen et al.[41] have since shown that chromatography can be applied to this system. The presence of chromatographic effects has apparently been recorded also in several other experimental investigations[45,46], in which study of the kinetics of the processes was not a matter of special concern.

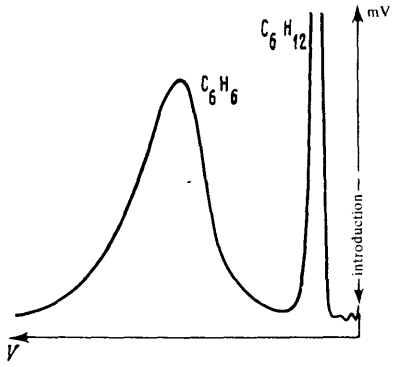


Figure 5. Chromatogram for the dehydrogenation of cyclohexane to benzene on a platinum–alumina catalyst.

2. Reaction of Type A ⇌ 2B

It has recently been shown[47] that reactions of the present type may also be influenced by chromatographic effects, although this cannot now be attributed to the spatial separation of molecules of the products on the bed of the microcatalytic reactor. Numerical calculations have again confirmed an increase in yield in the microreactor in comparison with the dynamic reactor, the difference gradually diminishing with increase in pulse width.

The increase in yield in this class of heterogeneous reactions is due to blurring of the product band resulting from the difference in adsorption coefficients between starting material A and reaction product B. This is entirely analogous to the above blurring of the product band for a first-order reaction. Nevertheless, the nature of the change in the yield occurring under non-stationary conditions in the present case is concealed in the differences between the adsorption coefficients Γ_A and Γ_B. When $\Gamma_A = \Gamma_B$, the effect should disappear.

Under the influence of diffusion the yield of the product may be higher than under stationary conditions even when $\Gamma_A = \Gamma_B$.[30] Since diffusion does not affect the rate of a first-order reaction, but diminishes the rate of reactions of higher order, the rate of the forward reaction will remain unchanged in the present case, whereas that of the reverse reaction ($n = 2$) will decrease. The yield of products B will therefore be higher than at equilibrium.

3. Consecutive Reactions

The main conclusion of the first kinetic analysis of a series of models of consecutive reactions[47] was that chromatographic effects could change significantly the selectivity of the catalytic process in comparison with a dynamic régime. For example, in both the reaction types

$$A \rightarrow B \rightarrow R \qquad R \rightarrow B \rightarrow S \quad (a)$$
$$A \rightarrow R \qquad 2R \rightarrow S \quad (b)$$

the yield y_R of the intermediate product R with a microcatalytic reactor might exceed tenfold the yield in a dynamic reactor. The yield y_R increases with decrease in the width of the entering pulse, since decrease in pulse width intensifies chromatographic effects.

These conclusions[47] were qualitatively confirmed by experimental investigations[48] on the cracking of cumene on an aluminosilicate catalyst in the microreactor. With a sufficiently narrow input peak of cumene yields of benzene exceeded the equilibrium values. The yield increased also when the microcatalytic bed was lengthened. By extrapolating the dependence of α on pulse width to zero, the reverse reaction (alkylation) can be neglected, and the rate constant can be calculated for the forward cracking reaction.

Cracking was accompanied by the disproportionation of cumene with the formation of di-isopropylbenzene[48]. The latter could occur in two possible ways:

$$\text{Cumene} + \text{Propene} = \text{Di-isopropylbenzene} \quad (c)$$
$$2\,\text{Cumene} = \text{Di-isopropylbenzene} + \text{Benzene} \quad (d)$$

In the case of reaction (c) a narrower pulse should give a lower yield of di-isopropylbenzene, since cumene and propene would then be more effectively separated. Since increasing the width of the sample has no effect on the yield of di-isopropylbenzene, it was concluded that catalytic disproportionation takes place in conformity with equation (d).

4. Reactions of Type A ⇌ B + C under a Chromatographic Régime

We have been considering the possible chromatographic effects under isothermal conditions of pulse developmental gas-adsorption chromatography. However, chromatographic separation can be accomplished in several ways[3], e.g. thermal displacement with a constant temperature field[49], chromathermographic[15], with a programmed rise in temperature[3], etc.

Let us consider, for example, the progress of the reaction A ⇌ B + C under the conditions of stationary chromathermography[50] suggested as long ago as 1950 to 1951 by Zhukhovitskii and Turkel'taub[51]. The essence of the method is that a band of material is moved along the bed of the stationary phase not only by a stream of carrier gas (as in the developmental form) but also by the simultaneous action of a moving temperature profile. This is usually accomplished by moving along the layer, in the same direction as the carrier gas, a furnace with a negative temperature gradient (i.e. a furnace in which the temperature is gradually raised will be advanced towards the bed at a speed w_n). The substance A introduced

orig inally into the microcatalytic reactor will be displaced along the charge, at a rate w_A inversely proportional to Γ_A, at the initial (low) temperature of the microreactor. No reaction will yet occur. During this initial period $w_n > w_A$, so that the band of A will gradually move into a region of higher and higher temperatures, which will accelerate its motion owing to the fall in Γ_A with rise in temperature.

At a certain "characteristic" temperature T_{char} the band of A will move along the layer at the same speed as the furnace. Zhukhovitskii and Turkel'taub showed that, under the conditions of stationary chromathermography, this temperature depends on the heat of adsorption Q_A and the linear rate of flow u of the carrier gas:

$$T_{char} = \frac{Q_A}{R \ln \frac{w_n}{u}} \quad (30)$$

At a given ratio w_n/u the characteristic temperature may be relatively low, and the reaction A ⇌ B + C will not take place. At a certain ratio w_n/u the characteristic temperature may be higher than the temperature T_{str} at which reaction begins. Migration of the band of A will then be accompanied by the formation of B and C, which will converge into zones corresponding to thei. characteristic temperatures $T_{char,B}$ and $T_{char,C}$. These features make chromathermography extremely promising for the attainment of considerable chromatographic effects. It must be emphasised that the reverse reaction C + B → A can be completely suppressed not only by the spatial separation of B and C on the bed in the microcatalytic reactor, as in the case of the isothermal pulse method, but also by the localisation of at least one of the products B or C (or their mixture) in a low-temperature zone. Thus even a reaction of type A ⇌ B can be conducted in one direction in a chromathermographic microcatalytic reactor.

Use of a chromathermographic microcatalytic reactor is sometimes advisable also because it always involves compression of the bands. Because a negative temperature gradient is present the front of the band, being situated in a cold region, moves more slowly than the rear portion, located in a hotter part of the bed. Since compression of the band entails an increase in concentration in the reaction zone, reactions above the first order must be expected to occur at higher rates than under isothermal conditions. In particular, reactions in which the products have smaller adsorption coefficients than the starting material, e.g. most cracking reactions, can be advantageously accomplished under such a régime.

A "thermal displacement" method can also be used in the absence of a stream of inert carrier gas[49]. Theoretical analysis shows[50] that movement of the furnace along the reactor causes the individual bands of starting materials and products to be situated along the catalyst bed in order of decreasing adsorption coefficients: i.e. the most sorbable substance will be "pressed" closest to the edge of the furnace, this will be followed by a less sorbable substance, and so on. In the case of the reaction A ⇌ B + C with $\Gamma_A > \Gamma_B > \Gamma_C$, for example, substance A will be converted, in the reaction zone adjacent to the furnace, into B and C, which will be removed continuously into the cold zone as adjacent bands of the pure substances. In this way a reversible reaction can be conducted in one direction.

The above considerations show that we are only at the very beginning of the study and the use of chromatographic effects in catalysis. There are grounds for supposing that further work on these lines will open up new prospects.

V. REACTIONS IN MICROREACTOR WITH A LANGMUIR ADSORPTION ISOTHERM

Above we have been considering reactions in the linear Henry range. The Japanese workers Hattori and Murakami[52] have discussed the kinetics of certain model reactions occurring in a microcatalytic reactor with Langmuir adsorption isotherms.

The equation of material balance for the ith component is written

$$\frac{\partial c_i}{\partial t} + q_{max.} \frac{\partial \theta_i}{\partial t} + u \frac{\partial c_i}{\partial t} + w_i = 0 \quad (31)$$

where q_{max} is the quantity of substance adsorbed when the surface is completely covered, θ_i the fraction of the surface occupied by the ith component, and w_i the rate of formation of this component. When equilibrium is established rapidly, the expression for θ_i has the usual form

$$\theta_i = \frac{\Gamma_i c_i}{1 + \sum_{i=1}^{n} \Gamma_i c_i} \quad (32)$$

where Γ_i is the adsorption coefficient of the ith substance. If adsorption equilibrium is reached slowly, equations of type (31) must be solved together with the kinetic equation

$$q_{max} \frac{\partial \theta_i}{\partial t} = w_{ai} + w_i \quad (33)$$

in which

$$w_{ai} = k_i^a \left\{ \left(1 - \sum_{i=1}^{n} \theta_i \right) c_i - \frac{\theta_i}{\Gamma_i} \right\} \quad (34)$$

and initial and boundary conditions are identical with those considered above for a linear isotherm.

The set of equations obtained after the introduction of dimensionless variables was solved by numerical methods for certain specific schemes.

1. Reaction A → R with Rapid Establishment of Adsorption Equilibrium

The dependence of the degree of conversion α on the length of bed was calculated in this case for different values of the parameter $\tau_0 = T/t_R$. Since T is the time of introduction of the pulse, and t_R the retention time of the initial substance, τ_0 is the dimensionless sample width.

It was found that α decreases with increase in τ_0, and reaches a minimum value as $\tau_0 \to \infty$, which corresponds to a flow-type reaction vessel. This result is easily explained by inhibition effects, which, of course, decrease with fall in concentration in the reaction zone. Blurring caused by the non-linearity of the adsorption isotherm is more marked and the degree of conversion is greater the smaller is τ_0. The difference between pulse and flow methods is due mainly to the decrease in concentration in the reaction zone.

2. Reaction A ⇌ R with Rapid Establishment of Adsorption Equilibrium

In this case, too, the degree of conversion is greater for the microcatalytic than for the dynamic reactor, owing to the diminished concentration resulting from blurring of the band. However, α cannot exceed the equilibrium degree of conversion, since blurring accelerates forward and reverse reactions to the same extent.

3. Reaction A ⇌ R + S with Rapid Establishment of Adsorption Equilibrium

For simplicity the case was considered [52] in which $\Gamma_A = \Gamma_S$ and $\Gamma_R = 0$. The degree of conversion in the microcatalytic reactor was shown to be lower than for the irreversible reaction A → R + S but considerably higher than for the reversible reaction A ⇌ R + S in a flow-type reaction vessel. The increase in α is due not only to a decrease in concentration in the pulse but also to chromatographic separation. Therefore the degree of conversion in the microcatalytic reactor increases with decrease in the width of the input pulse.

4. Reaction A → R with Slow Establishment of Adsorption Equilibrium

Differences between processes occurring in the microcatalytic reactor and the process in a dynamic reactor are still more clearly developed in this case, owing to the diminution in concentrations resulting from blurring of the peak and also from the difference in the initial surface coverage. In the microreactor the catalyst surface is unoccupied before the reactant is introduced, so that the rate of adsorption at the front of the band is high, as the denominator in the Langmuir equation is close to unity.

Since coverage in the first cross-section of the catalyst bed increases exponentially with pulse length, conditions can be selected [52] under which the difference in surface coverage between the pulse method and stationary conditions becomes insignificant. For "thin" pulses, however, the differences are very substantial.

Sadovnikov and Kislyuk note [53] that different conditions obtain in the pulse method and in the steady state when the catalytic reaction takes place at low surface coverage $\theta \ll 1$. Under stationary conditions this requires that $k^a < k^d$, but under pulse conditions small values of θ arise from the usual introduction of such a small quantity of starting material into the reactor that only a small part of the catalyst surface can be covered even on complete adsorption. Therefore the first order may be observed in the pulse method, but a fractional or even zero order under flow conditions.

Coverage of the portion of the catalyst bed on which the pulse is located depends also on k^a and k^d. It can be imagined that, when these constants are large (but equilibrium may still not be reached), the whole pulse is grouped on a very tiny part of the layer, where coverage is large. However, the situation described in Ref. 53 is also entirely possible. Unfortunately, to allow for all these factors quantitatively is quite a complicated task, since no analytical solution (even approximate) of the problem has been obtained, and the numerical calculations have been insufficiently detailed. A characteristic feature of this case would probably be variation in the order of the reaction with the volume of the sample at a constant initial concentration.

VI. KINETICS OF REACTIONS IN MICROREACTOR ON NON-UNIFORM SURFACES

Roginskii and Rozental' [54] analysed processes occurring on non-uniform surfaces (with respect to adsorption and catalytic properties) inside a microreactor. The equation

$$\frac{\partial\theta_A}{\partial t} = k_A^a c_A(1-\theta_A) - (k + k_A^d)\theta_A \qquad (35)$$

where θ is the relative coverage of active centres, applies to a group of sites having the same adsorption and catalytic properties. Applying the theory of catalytic processes on non-uniform surfaces [55], these workers obtained formulae for the quantity of substance adsorbed and the rate of the heterogeneous reaction. These enabled in principle equations for the form of elution curve of reactant A to be deduced from a known distribution function of sites with respect to adsorption and desorption rate constants $\rho(k_A^a, k_A^d)$. Analogous relations can be found also for the product B. Since a general solution of these equations presents considerable mathematical difficulty, certain particular cases were considered, for which quite simple expressions were obtained.

At low partial pressures (when $\theta_A \ll 1$), for example, the effect of non-uniformity for any distribution function $\rho(k_A^a, k_A^d)$ is merely to introduce an effective reaction rate constant calculated by means of the equation

$$k_{eff} = N_0 \int\int \frac{kk_A^d}{k_A^d - k}\rho(k_A^a, k_A^d)\,dk_A^a dk_A^d \qquad (36)$$

where N_0 is a constant depending on the number of active centres per unit surface, the specific surface, the density, and the porosity of the catalyst. An equation was obtained [54] enabling k_{eff} to be calculated from the measured quantity of unchanged substance $G(l)$, provided that the diffusion coefficient D was determined by an independent method. With low values of D the usual expression is obtained for a first-order reaction with a rate constant k_{eff} allowing for surface non-uniformity:

$$G(l) \quad G_0\exp-\left(\frac{k_{eff}l}{u}\right) \qquad (37)$$

Several other limiting cases were examined [54]. When adsorption equilibrium is established on every adsorption site, for example, the equations obtained have the same form as those for uniform surfaces. All the differences are covered by replacing the Henry coefficient and the rate constant of the heterogeneous reaction by integrated mean values for the non-uniform surface. Thus, with a known distribution function and a specified functional variation $k = k(\Gamma)$, the relations obtained for a uniform surface are easily generalised to apply to a non-uniform surface. The above cases by no means completely describe the processes occurring on non-uniform surfaces in a microcatalytic reactor. Future theoretical developments will probably enable the character of the surface non-uniformity with respect to adsorption and catalytic properties to be determined from the shape of the peaks of starting material or product measured under various experimental conditions.

VII. USE OF MICROREACTOR FOR DETERMINATION OF RATE CONSTANTS OF INDIVIDUAL PATHS IN COMPLICATED REACTIONS

It is clear from the above discussion of the kinetic features of the pulse method for studying catalytic reactions that quantitative analysis is at present possible only for relatively simple reactions. Detailed examination of the kinetics of complicated systems is as yet an unsolved problem. Nevertheless, even in this case, the use of a microcatalytic reactor may yield valuable information on the individual paths of a complex process. We shall confine the present Section to an analysis of the simplest cases of first-order reactions with rapid establishment of adsorption equilibrium and a linear adsorption isotherm.

The kinetics can be described approximately by the set of equations for steady-state operation of the reactor.

Before describing examples of the use of a microcatalytic reactor in investigating complicated catalytic reactions, let us consider briefly certain general aspects of the elucidation of formal kinetics from experimental data. Hitherto it has not been entirely clear [56-62] under what conditions all the paths of a complicated reaction can be determined with sufficient accuracy and the constants of individual transitions calculated from data obtained when all the processes in the system are occurring simultaneously. The main difficulty in the choice of the most probable mechanism for a complicated reaction is [58] that experimental errors do not permit differentiation between models yielding not greatly different calculated results. The position is considerably eased if statistical planning of the experiment [63] is used, but even then an unambiguous assessment of the adequacy of a model cannot always be expected.

The microcatalytic reactor has been used [64] to study the oxidative dehydrogenation of isopentenes to isoprene

$$2C_5H_{10} + O_2 \rightarrow 2C_5H_8 + 2H_2O \qquad (38)$$

on an iron–zinc–chromium oxide catalyst. The following assumptions were made on the basis of preliminary experiments and published information: (1) reaction (38) is irreversible, of first order with respect to the alkenes, and of zero order with respect to oxygen when it is in excess; (2) further oxidation to carbon monoxide and dioxide does not take place under the experimental conditions; and (3) isomerisation of the alkenes is described by a first-order equation. The above hypotheses are satisfied by the scheme in Fig. 6, which can be described by a linear set of equations.

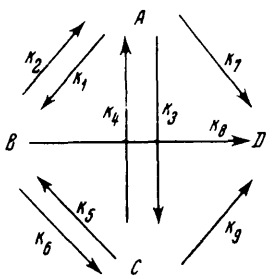


Figure 6. Scheme of interconversion in the oxidative dehydrogenation of isopentenes: A) 3-methylbut-1-ene; B) 2-methylbut-1-ene; C) 2-methylbut-2-ene; D) isoprene.

The initial rates wA, wB, wC, and wD were determined graphically [64] by differentiating the initial portions of the rate curves obtained for each set of compositions. Initial mixtures were prepared with compositions corresponding to the planning matrix of the complete factorial experiment [63]. Using as a first approximation the constants obtained by planning the experiment, more accurate values were found from the condition that differences between calculated and experimental partial pressures should be minimal. The values were refined from the experimental kinetic curves by the method of steepest descents [65]. This yielded for the rate constants (in s^{-1}) the values

$$k_5 = 12.8 \pm 0.4; \quad k_6 = 5.5 \pm 0.2;$$
$$k_7 = 0.7 \pm 0.2; \quad k_8 = 3.7 \pm 0.2;$$
$$k_9 = 1.1 \pm 0.1.$$

The values of k_1–k_4 in Ref. 64 were small. Since equating each of the constants to zero produced only an insignificant change in the calculated concentrations, it was impossible to determine their exact values. It was established, however, that $k_3 > k_1 > k_2 > k_4$. Additional kinetic experiments with the pure isomers were necessary in order to establish this sequence.

A microcatalytic reactor has been used also [66] to study the oxidative dehydrogenation of pentenes under conditions such that further oxidation of the pentenes and of isoprene also occurred. A set of differential equations was written on the above hypotheses that all reactions were of the first order, and these were solved by two methods—approximate integration by means of Simpson's formula [67] and numerical integration on an M20 computer—the rate constants being so chosen that concentrations calculated on the electronic computer approached as closely as possible to the experimental values. Good agreement was obtained between results obtained by the two methods.

VIII. USE OF MICROREACTOR AND RADIOCHROMATOGRAPHY FOR STUDY OF COMPLICATED CATALYTIC CONVERSIONS

Mathematical models evidently do not always give a clear and reliable criterion for distinguishing between particular schemes for a complicated process. The additional information usually employed for sifting certain hypothetical schemes is extremely useful. In order to select the most probable reaction scheme we must investigate the agreement between the chosen model and experiment with a wide variation in the experimental parameters. In this respect broad possibilities are opened up by combining the microcatalytic reactor with radiochromatography. The first attempt to do this was made in the fundamental work by Emmett and his coworkers [1]. However, these workers were unable to make any quantitative estimates of rates. Significant progress can be made by combining the microcatalytic reactor with the kinetic isotope method, which was suggested by Neiman more than fifteen years ago [68-70].

This latter combination of methods was first applied by Roginskii et al. [71-75] in studying the oxidative dehydrogenation of butenes to butadiene. The possible reactions can be represented by Fig. 7, in which [A]–[D] are the concentrations and α–δ the specific radioactivities of but-1-ene, *trans*-but-2-ene, *cis*-but-2-ene, and butadiene respectively. Three series of experiments were made by introducing into the microcatalytic reactor mixtures of two components of specified chemical and radiochemical composition—(I) butadiene + *cis*-[^{14}C]but-2-ene, (II) but-1-ene + *cis*-[^{14}C]but-2-ene, and (III) but-1-ene + *trans*-[^{14}C]but-2-ene—by the method of impinging pulses [75]. The concentrations of A–D and the specific radioactivities α–δ were determined by radiochromatographic analysis [76-78].

If all stages of the scheme had been reversible, the specific radioactivity of *trans*-but-2-ene would have been given by [70]

$$\frac{d\beta}{d\tau} = \frac{\delta-\beta}{[B]} w_{D-B} + \frac{(\gamma-\beta)}{[B]} w_{C-B} \frac{(\alpha-\beta)}{[B]} w_{A-B} \qquad (39)$$

where w_{D-B}, w_{C-D}, and w_{A-B} are the rates of conversion of butadiene, *cis*-but-2-ene, and but-1-ene respectively into *trans*-but-2-ene. Experiment showed that $d\beta/d\tau \simeq 0$. Further, it can be assumed with a certain approximation that $\gamma - \beta \simeq 0$ and $\alpha - \beta \simeq 0$. Since $\delta - \beta \neq 0$, Eqn. (39) is valid only when

$$w_{D-B} = 0;\ w_{D-A} = 0;\ w_{D-C} = 0$$

i.e. hardly any butene was formed from butadiene in the above experiments.

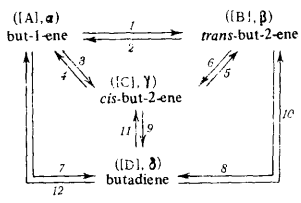


Figure 7.

Experiment showed that $w_{C-D} > w_{C-A}$. The variation in specific radioactivities found experimentally indicates that *trans*-but-2-ene and butadiene obtained from *cis*-[^{14}C]but-2-ene are diluted with but-2-ene and butadiene formed from but-1-ene:

$$\frac{d\beta}{d\tau} < 0 \qquad (40) \qquad\qquad \frac{d\delta}{d\tau} < 0 \qquad (41)$$

It was shown that butadiene was diluted considerably more strongly. Hence it follows that

$$w_{A-D} > w_{A-B}$$

Inspection of the curves obtained for series (III) indicated that the *cis* → *trans* isomerisation was more rapid than the reverse process:

$$w_{C-B} > w_{B-C} \qquad (42)$$

and also that

$$w_{C-D} > w_{B-D} \qquad (43)$$

Experiments were made with ternary systems (but-1-ene + *cis*-[^{14}C]but-2-ene + butadiene) in order to determine the immediate precursors of butadiene. The specific radioactivity of butadiene has a maximum value, which is lower than the specific activity of *cis*-[^{14}C]but-2-ene at time τ_{max}:

$$\delta_{\tau_{max}} < \gamma_{\tau_{max}} \qquad (44)$$

This implies that *cis*-but-2-ene is not the sole precursor of butadiene in the system. The ratio $\gamma\tau_{max}/\delta\tau_{max}$ indicated that the rate of formation of butadiene from but-1-ene was about double the rate from *cis*-but-2-ene:

$$w_{A-D} \approx 2w_{C-D} \qquad (45)$$

Radiochromatography has been combined with a microcatalytic reactor in order to estimate the six rate constants for the interconversion of but-1-ene, *cis*-but-2-ene, and *trans*-but-2-ene on an aluminosilicate catalyst [79].

A microcatalytic reactor has been combined with radiochromatography to study the oxidative dehydrogenation of butenes on a bismuth–molybdenum catalyst, the results being processed on an electronic computer [80]. Finding the kinetic constants encountered considerable difficulty owing to the simultaneous occurrence under the experimental conditions of nine separate reactions of isomerisation and mild oxidation, as in the study of the oxidative dehydrogenation of isopentenes (Fig. 6). The kinetics of oxidative dehydrogenation could be represented by a set of differential equations. Statistical planning of experiments [63] and non-linear programming [81] were also used. The preliminary values of the constants calculated by this method were then refined [80] using Neiman's kinetic isotope method and a microcatalytic reactor.

Rate constants for the conversion of stable compounds are determined in the kinetic isotope method by the simultaneous solution of the material balance equations of the reactants in terms of concentration and radioactivity. If the complete reaction scheme has been chosen correctly, the rate constants obtained should describe accurately the variation in the specific activities of the products with time.

If the specific radioactivities of but-1-ene, *trans*-but-2-ene, *cis*-but-2-ene, and butadiene are denoted by α, β, γ, and δ (Fig. 7), it can be shown by Neiman's method that the variation in the specific radioactivities of these hydrocarbons is represented by the equations

$$\frac{d\alpha}{dt} = \frac{1}{[A]}\{k_4[C](\gamma - \alpha) + k_2[B](\beta - \alpha)\} \qquad (46)$$

$$\frac{d\beta}{dt} = \frac{1}{[B]}\{k_1[A](\alpha - \beta) + k_5[C](\gamma - \beta)\} \qquad (47)$$

$$\frac{d\gamma}{dt} = \frac{1}{[C]}\{k_3[A](\alpha - \gamma) + k_6[B](\beta - \gamma)\} \qquad (48)$$

$$\frac{d\delta}{dt} = \frac{1}{[D]}\{k_7[A](\alpha - \delta) + k_8[B](\beta - \delta) + k_9[C](\gamma - \delta)\} \qquad (49)$$

Comparison of experimental and calculated specific radioactivities of products of oxidative dehydrogenation at 396°C (for the series but-1-ene + *cis*-[^{14}C]but-2-ene).

Time of contact, s	But-1-ene		*trans*-But-2-ene		*cis*-But-2-ene		Butadiene	
	expt.	calc.	expt.	calc.	expt.	calc.	expt.	calc.
0.0065	9.4	9.4	92.0	92.0	155	155	20.0	20.0
0.0090	11.0	12.7	93.0	93.0	151	152	30.0	32.8
0.0118	15.0	16.3	94.0	95.2	149	149	39.0	42.8
0.0144	17.5	19.5	94.5	97.0	145	146	48.0	50
0.0190	23.0	25.0	96.0	98.0	140	141	58.5	59.6

These were solved together with the equations of material balance, and the rate constants were calculated with an electronic computer from the condition that the calculated curves for the variation in concentrations and specific activities with time should be close to the experimental curves. The Table shows agreement between experimental and calculated values of the specific activities of the components for various contact times.

Rate constants determined by means of a microcatalytic reactor combined with Neiman's kinetic isotope method were given [80] for the individual reaction paths in the oxidative dehydrogenation of butenes to butadiene. The dehydrogenation of but-1-ene was the most rapid (especially at low temperatures). At high temperatures the oxidative dehydrogenation of *cis*- and *trans*-but-2-enes also becomes appreciable.

A promising approach was shown [80] for combining computer processing of kinetic curves obtained by means of a microcatalytic reactor with continuous checking of the results by radiochromatography. This makes calculation of the constants less formal, and also reduces considerably the volume of laborious and complicated isotopic experiments.

IX. PULSE METHOD FOR STUDY OF POISONING OF CATALYSTS

The poisoning of catalysts by various poisons is usually studied with the aim of obtaining information on the number and nature of the active centres. Pulse methods have recently begun to be used to study poisoning [82,83]. This usually involves introducing, into a stream of an inert carrier gas entering the reactor at the reaction temperature, a fixed dose of the poison, which is adsorbed on the catalyst surface. After this the activity of the poisoned catalyst is studied, also by a pulse method. This method of study was probably first applied to the dehydrogenation of butane to butenes and butadiene [7]. Turkevich et al. [82] introduced several successive doses of the poison into the reactor in order to study the dependence of the activity of the catalyst on the dose. However, it then emerged [83] that under pulse conditions catalyst poisoning is a transient process, and therefore irreproducible results may be obtained. The method was subsequently developed by Romanovskii, Topchieva, and their coworkers [83-85].

Until recently no theoretical examination had been made of poisoning in a pulse reactor. Romanovskii [86] pointed out that, for non-linear laws of poisoning, not only the quantity of poison absorbed by the catalyst surface but also its distribution along the bed are significant.

A quantitative theory of the pulse poisoning of catalysts has recently been developed [87,88] taking into account the adsorption characteristics of the poison. Two types of centres are supposed to be present on the catalyst surface. A first-order heterogeneous catalytic reaction takes place on the first group of centres; the starting material may be adsorbed reversibly on the second group, but this does not involve any reaction. It is assumed also that the poison is adsorbed considerably more firmly than the initial substance, and that adsorption of the poison is described by the Langmuir equation.

On the basis of the above model, equations were obtained for the time variation of catalytic activity after introduction of the poison. With reversible adsorption of the poison, the activity of the catalyst first falls, reaches a minimum value, and then gradually increases to the original level. The initial fall in catalytic activity is due to the fact that the poison is located entirely on the catalyst bed. The chromatographic band of the poison is blurred, and its molecules are redistributed between catalytic and adsorption centres. When the poison band reaches the outlet from the reactor, the activity of the catalyst increases, to reach its original value when the last poison molecules leave the reactor.

With an exponential law of poisoning the descending portions of the curves can be represented by the equation

$$\frac{A_g}{A_0} = y + 1 - (\sqrt{\mu} + \sqrt{y})^2 + \int_{y}^{(\sqrt{\mu}+\sqrt{y})^2} \exp - \nu_k \frac{\beta\left(\sqrt{\frac{z}{y}} - 1\right)}{1 + \beta\left(\sqrt{\frac{z}{y}} - 1\right)} dz \qquad (50)$$

and the ascending portions by the formula

$$\frac{A_g}{A_0} = y + \int_{y}^{1} \exp - \nu_k \frac{\beta\left(\sqrt{\frac{z}{y}} - 1\right)}{1 + \beta\left(\sqrt{\frac{z}{y}} - 1\right)} dz \qquad (51)$$

where $A_0 = \lg(1 - \alpha_0)^{-1}$ is the initial activity of the catalyst, α_0 the degree of conversion of the reactant before introduction of the poison, A_g the activity of the poisoned catalyst, $y = t/t_{max}$ the dimensionless time, t the time, t_{max} the time of complete regeneration of the catalyst, $\mu = m_0/q_{max}$ the reduced dose of poison, m_0 the quantity of poison introduced into the reactor, q_{max} the quantity of poison required for a monolayer, b_K the adsorption coefficient of the poison on the active centres, b the mean adsorption coefficient of the poison on catalytic and adsorption centres, and ν_K the number of poison molecules which can be adsorbed on one active centre in the catalyst surface.

The position of the minimum y_{min} in the experimental dependence of the relative activity of the catalyst on the dimensionless time can be used to determine q_{max}:

$$q_{max} = \frac{m_0}{(1 - \sqrt{y_{min}})^2} \qquad (52)$$

The mean adsorption coefficient of the poison b is determined from the time of complete regeneration of the catalyst:

$$b = \frac{v \cdot t_{max}}{q_{max}} \qquad (53)$$

where v is the space velocity of the carrier gas. Furthermore, the most probable law of poisoning can be selected from a comparison of calculated and experimental results, and the ratio of the adsorption coefficients β determined. The adsorption coefficient of the poison on the active centres is then found from the simple relation

$$b_k = b\beta \qquad (54)$$

The above theory of pulse poisoning has been verified in a study [88] of the poisoning by pyridine of an aluminosilicate catalyst for the cracking of cumene. Values of b and q_{max} calculated from the time variation of activity during poisoning were compared with direct measurement of the adsorption of the poison on the catalyst under the same conditions. Satisfactory agreement was obtained.

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The information reviewed above shows that the pulse chromatographic method can be successfully applied to the solution of many problems in the field of catalysis. The range of application of the method has been continuously extended as the theory of the method has been improved. It must be borne in mind, however, that, since the method is transient, difficulties inevitably arise in processing the measurements, especially in the case of non-linear adsorption isotherms.

An attempt to avoid these difficulties led to a second form of the pulse method, in which a broad rectangular pulse, whose front and rear edges are as sharp as possible, is introduced into a relatively small reactor [89]. The idea is that, by introducing a "wide" pulse, it can be assumed that adsorption–chemical equilibrium is established, and the process can be regarded as stationary–microdynamic.

The results can now be processed by methods adopted in work with a flow-type reactor. When the properties of the catalyst vary slowly with time, it is possible to examine the effect of the reaction medium on the properties of the active surface. A weak point in the method is some arbitrariness in the choice of pulse width, which must correspond to the rate of establishment of adsorption–chemical equilibrium. However, it is not always a simple matter to estimate the rate of adsorption and desorption during catalysis. In particular, such a method may lead to errors in the case of slow irreversible chemisorption on the layer of catalyst. It must be remembered that the use of wide pulses is suitable mainly in work with low concentrations of the starting material, since, when a wide pulse with a high partial pressure of the starting material is introduced into the microreactor, it can no longer be always assumed that the properties of the catalytic surface remain unchanged during passage of the pulse along the catalyst bed.

A significant advance is the recently proposed[90] gradient free pulse method, in which the pulse of reactant is introduced into a microreactor containing a pseudo-fluidised bed of the catalyst. This has the advantage over the preceding method that, because of the absence of gradients, the reaction velocity can be measured directly under specified experimental conditions. However, this method is not free from the defects inherent in the above "microdynamic method"—those involving the choice of sample size and the need to work with low concentrations of the starting material.

In the present paper we have wanted to show that the theory of transient processes occurring under pulse conditions has recently been undergoing vigorous development. Such development has been stimulated by the great opportunities for pulse methods in the study of the kinetics and the mechanism of transient processes.

The chromatographic technique will yield information which it is sometimes impossible to obtain by traditional methods. In our opinion it is not necessary to strive to replace stationary by pulse methods. These methods should be used to solve different problems, supplementing each other.

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Institute of Chemical Physics,
USSR Academy of Sciences,
Moscow

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Advances in the Coordination Chemistry of Azoles

A.D.Garnovskii, O.A.Osipov, L.I.Kuznetsova, and N.N.Bogdashev

A systematic account and review of the literature on complexes of azoles is given. Particular attention has been devoted to the problem of the location of the coordinate bond in the azole molecule, competitive coordination in ambident azole-containing systems, elementotropism in a series of *N*-element derivatives of azoles, and the polyhedral forms of chelate complexes in the azole series.
The bibliography includes 508 references.

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I. INTRODUCTION

In 1958 Dorothy Hodgkin's group summarised[1] the results of almost ten years work on the elucidation of the structure of vitamin B_{12} for which the Nobel Prize was subsequently awarded. The authors established that, in contrast to nucleic acid nucleotides, in the B_{12} nucleotide the base (skeleton) is not a purine or pyrimidine but the cobalt complex of 5,6-dimethylbenzimidazole[2,3]. More than anything else, this discovery[4] and also earlier data concerning the involvement of azole systems in the biochemical binding of metals (haemoglobin, cytochromes, etc.)[5] served as a powerful stimulus for the development of synthetic, physicochemical, and structural studies on metal complexes of azoles and their derivatives. This idea is confirmed by the finding that, whereas up to the end of the 1950's occasional synthetic or analytical studies were made on azole complexes[6-8], in the 1960's and the 1970's azole-containing systems began to occupy leading positions among nitrogen-containing ligands[9].

In the present review, a systematic account is given of data for different types of complexes formed by azole-containing ligands: (1) molecular complexes; (2) *N*-metal and *N*-element derivatives of azoles; (3) chelate complexes.

The review does not claim to give an exhaustive coverage of all data on azole complexes but it does include the main advances in the synthetic and structural chemistry of complexes of azole-containing systems during the last decade (1961–1971 and partly 1972).

II. MOLECULAR COMPLEXES OF AZOLES

The presence of several heteratoms in the quasiaromatic π system suggests that azoles can behave as polydentate ligands. Therefore the most important problem in the chemistry of the complexes of azole-containing systems is the site of the coordinate bond (competitive coordination[10]). Hitherto, this problem has not been unambiguously solved.

It is believed that, depending on the type of azole, metal, and reaction conditions, the coordinate bond may be located at the pyridine-type nitrogen atom [4,6,9-27], the oxygen or sulphur heteroatom [28-31], or the π system [32-36]. On the other hand, analysis of numerous literature data suggests that azoles are monodentate ligands† with a single centre where the coordinate bond is located—the nitrogen atom of the pyridine type. This conclusion has been justified not only theoretically [9] (by the finding of the maximum π-electronic charge at the pyridine nitrogen atom) but also by direct X-ray diffraction studies [36-40] and by NMR, [41] infrared [18,22,42-44], and ultraviolet [24] spectroscopy. The conclusion that transition metals may be coordinated to the oxygen atom of the oxazole ring [29,30], reached by Duff on the basis of infrared spectroscopic and magnetochemical studies of benzoxazole complexes, has little evidence to support it. Pyl's attempts [28] to account for the unusual properties of thiazolylformazan by the coordination of the metal to the sulphur atom of the thiazole ring is also unconvincing. Finally there is no rigorous evidence for the possibility of complex formation involving the π system of the azole rings: even typical π-complex forming agents, such as metal carbonyls, form with azoles predominantly σ complexes and not π complexes [9,34,35,45-48].

1. COMPLEXES OF AZOLES WITH GROUP I, II, VII, AND VIII BIVALENT METALS

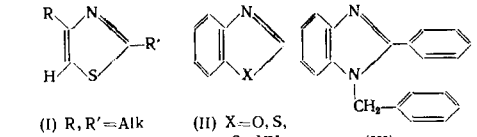
The greatest number of studies have been made on the physicochemical properties and structures of the coordination compounds of monodentate azoles with metal (II) salts‡. In most cases complexes of this type are synthesised by heating the components in ethanol [49-66]. Sometimes methanol [25,26,67-69] and acetone [27,50,63,70] are used for this purpose or the azoles are fused together with metal halides [20]. However, these procedures yielded complexes containing a large number of ligand molecules. Therefore, to synthesise complexes with a low coordination number (C.N.) of the metal, the above complexes were decomposed *in vacuo* at 90–140°C. [31,55,64] The composition of the complexes varies from $MX_2.L$ to $MX_2.6L$ and depends mainly on the stoichiometry of the reactants.

The basicity (pK_a) of azoles has almost no influence on the coordination number of the metal: coordination compounds with compositions ranging from $MX_2.L$ to $MX_2.6L$ may be obtained both for imidazole ($pK_a = 7$) [9,71] and for tetrazole ($pK_a \simeq 0$). [72] Similarly in the series of *C*- and *N*-alkyl substituted pyrazoles, complexes with the composition $MX_2.nL$ ($n = 2-4$) have been obtained [23] regardless of the basicity (the pK_a varied from 4.12 to −1.96). However, in the series of benzazoles the effect of basicity on composition is fairly clear: complexes of the type $MX_2.4L$ are readily obtained for benzimidazole ($pK_a = 5.53$), [9] the less basic benzothiazole ($pK_a \simeq 2.0$) [9] forms coordination compounds having the above composition only with a limited number of metals and anions, and benzoxazole ($pK_a \simeq 1$) [9] forms complexes which do not contain more than two ligand molecules.

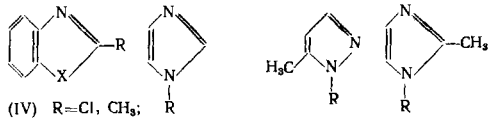
The metal has also little influence on the composition. Coordination compounds with the composition $CuX_2.6L$ cannot be isolated in most cases only for copper salts, although such complexes are known for imidazole [49] and its 4(5)-bromo-derivative [73].

The effect of anions and steric factors, which depend on the steric effectiveness of the ligand structure, on the composition of the coordination compounds is much more significant. Metals linked to ClO_4^- and BF_4^- show the greatest coordination capacity (complexes $MX_2.4L$ are formed), while NO_3 and NCY (Y = O, S, or Se) reduce the coordination number of the metal owing to their largely bidentate properties.

The introduction of bulky substituents into the ligand molecule reduces the number of coordinated azoles. Thus the complexes $MX_2.2L$ have been described [57,74] for alkyl-substituted thiazole (I). Benzo-analogues of azoles (II) form complexes which do not contain more than four ligand molecules even in the presence of the perchlorate anion [59,63]. On further increase of the complexity of the ligand, coordination compounds containing not more than two azole molecules are obtained, for example with 1-benzyl-2-phenylbenzimidazole (III). [75] In most cases other complexes, obtained with ligands containing in the 2-position of the azole ring substituents less bulky than the phenyl group [compounds (IV)], have the same composition [25,26,29,67,76,77].



(I) R, R′=Alk (II) X=O, S, Se, NH (III)



(IV) R=Cl, CH_3; X=O,S, NH (V) R=CH_3, n-C_4H_9 (VI) (VII) R=H, CH_3.

The above considerations concern only *C*-alkyl or *C*-aryl substituted derivatives in which the substituent gives rise to steric hindrance at the reaction centre (the pyridine-type nitrogen atom). On the other hand if the substituents are remote from the centre where the coordinate bond is located, the composition of the complexes is similar for substituted and unsubstituted azoles. This is probably the explanation of the finding that *N*-alkyl-substituted imidazoles (V) form $MX_2.6L$ complexes even in the presence of the bulky butyl substituent [44,78], while 5-methylpyrazole (VI) forms in addition [79] a complex with seven ligand molecules§. On the other hand, coordination compounds not containing more than four azole molecules have been described for 2-methylimidazole (VII, R = H) [73] and 1,2-dimethylimidazole (VII, R = CH_3). [70,80].

The type of polyhedra formed by azole complexes depends mainly on the coordination number of this metal and its electronic configuration, the nature of the anion and the ligand, and in many cases on the state of aggregation of the system. The complexes $MX_2.4L$ and $MX_2.6L$ have an octahedral structure with some distortion along the tetragonal axes due to the specific influence of the ligand and the anion.

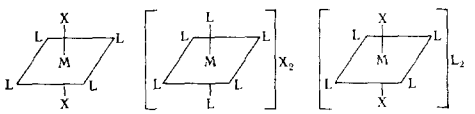
† Azoles containing in the heterocyclic nucleus several sp^2-hybridised nitrogen atoms behave as bridge-type bidentate ligands (see below).

‡ Data for complexes of the most important azole-containing systems have been tabulated [9].

§ In the complex $MX_2.7L$ [L = (VI)], one of the ligand molecules is partly linked as a solvating species [79].

Usually, but not necessarily, coordination compounds of the type $MX_2.4L$ have a *trans*-octahedral structure (VIII). Distortion of the latter can lead to an elongated or shortened tetragonal bipyramid [81,82] and also to a tetrahedral configuration with weakly bound anions located along the tetragonal axes [68]. On the other hand, planar square polyhedra are also encountered among complexes of this type. These are characteristic of nickel [49,58,83] coordination compounds with I^-, ClO_4^-, BF_4^-, and NCS^- anions and of palladium [31] complexes with Cl^-, I^-, and NO_3^-.

The fundamental problem concerning the $MX_2.6L$ complexes is that of the octahedron formed: $[ML_6]_2X_2$ (IX) or $[MX_2L_4]L_2$ (X): [49]



X-Ray diffraction [39,84] and spectroscopic [16,24,49,85] studies led to an unambiguous solution in favour of structure (IX) in which the metal is surrounded by six atoms of pyridine-type nitrogen. The polyhedral forms of the complexes $MX_2.2L$ are much more varied.

The electronic configuration of the metal in this type of coordination compound frequently plays a decisive role: mainly tetrahedral complexes are formed by Co^{II} (d^7) and Zn^{II} (d^{10}), planar and octahedral complexes are formed by Ni^{II} (d^8) and Cu^{II} (d^9), and only planar complexes are formed by Pd^{II} (d^8). However, this postulate cannot be regarded as valid without exception since among cobalt and zinc complexes coordination complexes are encountered with an octahedral structure [27,55] and there are tetrahedral copper and nickel complexes [19,58]. These deviations are associated primarily with the nature of the anions among which mention should be made of I, NCY (Y = O, S, or Se), and NO_3, which exhibit specific effects. When chlorine and bromine in the nickel complexes of imidazole [20], its 5-bromo-derivative [73], and benzoxazole [19] of the type $NiX_2.2L$ (X = Cl or Br) are replaced by iodine, there is a change from an octahedral to a tetrahedral coordination. On the other hand, in the 2-methylimidazole complexes the octahedron → tetrahedron transition is observed not only for nickel iodide but also for the bromide.

The replacement of chlorine and bromine by iodine frequently leads to a flattening of the tetrahedral configuration. The tetrahedron → planar square transition is characteristic of complexes of nickel halides with 1-benzyl-2-phenylbenzimidazole [75] and 2-aminobenzothiazole [86]. The structural characteristics of such complexes can be accounted for by the different degrees of polarisability of the halogens (I > Br > Cl) and their different sequence in terms of their effective contribution to the metal–ligand π-dative bond [87].

The specific effect of the NO_3^- and NCY^- groups is due to the fact that the nitrate ion frequently behaves as a bidentate ligand [88-91] and pseudohalide anions form bridge-type structures [9,10,92-95]. As a result, both anions increase the coordination number of the metal in the complexes $MX_2.2L$ to six and promote the formation of octahedral structures. The transition from tetrahedral and planar configurations to the octahedral configuration, which is frequently observed [19,50,64,81,96,97], was discussed in detail by Duff and coworkers for benzothiazole and benzoxazole complexes of transition metal nitrates [65]. The infrared and Raman spectra of these complexes show M–O bond vibration frequencies in the low-frequency region (at 270–350 cm^{-1}), which vary with the nature of the metal and the ligand. On the other hand, there have been a number of studies where it has been shown convincingly that the NO_3^- anion can also behave as a monodentate ligand. In this case, when complexes are formed with nitrate, the type of polyhedra formed by the $MX_2.2L$ coordination compounds remains the same [4,27]. Pseudohalide ions behave in the same way, since among the complexes $MX_2.2L$ containing the NCY^- anions not only bridge-type octahedral but also planar [75,76,98,99] and tetrahedral [27,63,77,100] structures are encountered. In the latter case the question of the mode of coordination of the pseudohalide ion is usually discussed and a decision in favour of the M–N bond is made for the azole complexes [27,44,63,76,77,98-100] on the basis of the generally accepted tests [9,10,92-94,101].

For the same composition, metal, and anion, it is possible to follow the influence of the fine structure of the ligand on the structure of the coordination compound. Thus, in contrast to the planar complexes of nickel thiocyanate with 2-methylbenzimidazole [76], the analogous benzimidazole complexes are octahedral [102]. Nickel chloride complexes of the type $MX_2.2L$ are tetrahedral with benzimidazole [60], while those with benzothiazole [63] and benzoxazole [19] are octahedral.

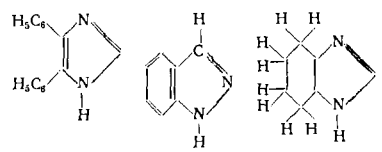
The amount of data available for the interpretation of the structures of the azole complexes of the type $MX_2.L$ and $MX_2.3L$ is much less. Depending on the electronic structure of the metal, planar (copper [31,55,63]), octahedral (nickel [20,31,61,63] and cobalt [20,55]), or tetrahedral (cobalt [20,31] and zinc [31]) configurations are attributed to complexes of the first type. Trigonal-bipyramidal [70] or polymeric-octahedral [29,57] configurations are postulated for $MX_2.3L$ coordination compounds. Rigorous proof has been obtained only for the 1,2-dimethylimidazole complex of copper(II) chloride: X-ray diffraction analysis definitely indicates a *cis*-trigonal bipyramidal structure [103]. Bearing in mind that in many cases the configuration of the complexes may alter in solution [9,104,105], the data quoted in this section must be treated with some caution. Whereas one can hardly expect a change in the form of the polyhedron on dissolution of coordination compounds of the type $MX_2.6L$ and $MX_2.4L$, the changes in the polyhedral forms of certain azole complexes of the type $MX_2.2L$ are very significant (as already shown above) [19,27,99].

The stability of the azole complexes of the type discussed above has not been the subject of systematic studies. Most data are available for the stabilities of the complexes of imidazole [106-114] and some of its derivatives [115,116]. Sklenskaya and Karapet'yants [114] determined the thermodynamic functions for the formation of complexes by bivalent copper, nickel, and cobalt ions with imidazole in aqueous solutions from measurements of the temperature variation of the instability constants in the range 10–50°C. They established that the instability constants of the imidazole complexes and the ΔH_1 vary in the sequence Cu > Ni > Co, which is the same as the Irving–Williams stability series generally adopted for nitrogen-containing ligands [117]. The ΔH_1 agree with the values found calorimetrically (7.6 kcal $mole^{-1}$ for copper and 5.8 kcal $mole^{-1}$ for nickel), the values for the imidazole complexes being significantly higher than for the ammines (5.6 kcal $mole^{-1}$ for copper and 4 kcal $mole^{-1}$ for nickel) [118].

2. COMPLEXES OF AZOLES WITH THE HALIDES AND TRIALKYL DERIVATIVE OF GROUP III ELEMENTS

With the exception of scandium coordination compounds, complexes of azoles with MX_3 (M = B, Al, Ga, In, Tl, or Sc and X = Cl, Br, I, or CH_3) are synthesised in aprotic absolute solvents [9,119-125]. The comparatively high stability of scandium halides and their complexes makes it possible to synthesise the latter in ethanol [121]. The trihalides of boron [119,126], aluminium [120,121], and gallium [9,119] and their trimethyl derivatives [119,122] form mainly 1 : 1 complexes with azoles, while the compositions $MX_3.2L$ and $MX_3.3L$ are more characteristic of the corresponding indium [9,119,123,124], thallium [125], and scandium [121] coordination compounds. This result is apparently due to the fact that a tetrahedral structure with an sp^3-hybridised metal atom is most characteristic of the boron, aluminium, and gallium complexes, while an octahedral or a trigonal-bipyramidal structure (with d^2sp^3 and sp^3d-hybridisation respectively) is typical for indium, thallium, and scandium coordination compounds [9,104,127-129].

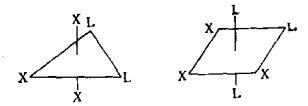
As for the azole coordination compounds with bivalent metals, the compositions of complexes of azole ligands with MX_3 depends more on the bulk than on the basicity of the ligand. Thus, whereas up to 4 (indium chloride [123]), 5 (aluminium bromide [120] and indium iodide [123]), and 6 (aluminium chloride [119,121] and scandium chloride [121]) molecules of imidazole(V), which has a relatively small bulk and a high basicity, combine with the metal halides, the number of coordinated molecules of the bulky 4,5-diphenylimidazole (XI), which has a similar pK_a, does not exceed unity for AlX_3 [9,119-121] or two for InX_3. [119,123] In the series of benzimidazole, pyrazole, and indazole (XII) derivatives, the basicity decreases while the composition remains unchanged ($InX_3.3L$). [123]



(XI) (XII) (XIII)

On the other hand, the increase of the basicity of certain imidazole derivatives with analogous structures is accompanied by an increase of the number of coordinated ligand molecules in the complex. Depending on the reactant ratio, aluminium bromide [120] and chloride [121] and scandium chloride [121] can combine with up to five molecules of tetrahydrobenzimidazole (XIII), while in the complexes with benzimidazole (IV, X = NH, R = H) the maximum number of coordinated molecules does not exceed three. Similarly indium trichloride and tri-iodide form complexes having the composition $InX_3.4L$ with (XIII) and $InX_3.3L$ with (IV, X = NH, R = H).

In order to obtain information about the structures of coordination compounds, studies have been made [9,119-123] on the infrared absorption spectra of the complexes and their dipole moments have been determined; infrared, Raman, and ESR spectra have been studied by Cotton and Gibson [124], mass spectrometric, NMR, and vibration spectra by Lee [125], and NMR spectra by Fratiello [126]. The stretching vibration frequencies of the azole rings were found to increase in the infrared spectra of complexes of the type $MX_3.nL$ ($n = 1-6$) which suggested [9,119-123] that the coordinate bond is located at the pyridine-type nitrogen atom of the heterocycle. In addition to this frequency increase, the infrared spectra of the coordination compounds $MX_3.nL$ (M = Al or B, $n > 1$; M = In or Sc, $n > 3$) showed bands due to non-coordinated ligands. On this basis, a solvate structure of the type $[MX_3.(n-m)L]mL$ was attributed to these coordination compounds [9,119-121,123]. One cannot rule out the possibility of the formation of solvates also in the case of gallium complexes of the type $GaCl_3.2L$, although the coordination capacity of this metal is consistent with the formation of trigonal-bipyramidal coordination compounds (sp^3d hybridisation). On the basis of the infrared spectra and the dipole moments, which vary in the range 4-7 D, a *cis*-trigonal-bipyramidal configuration (XIV) was attributed to the complexes $InX_3.2L$ and a *cis*-structure with C_{2v} symmetry (XV) was attributed to octahedral coordination compounds of the type $InX_3.3L$:



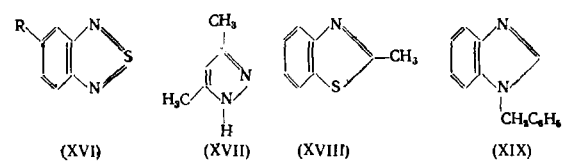
(XIV) (XV) [9,119,123]

A comparative estimate of the stabilities of the complexes was made from the frequency shifts of the stretching vibrations of the azole rings ($\Delta\gamma$). It was found that the $\Delta\gamma$ for the MX_3 complexes of the same composition and structure are satisfactorily correlated with the basicities of the azole ligands [9].

The conclusions based on the infrared spectroscopic studies have been confirmed in a few cases also by measurements of the dipole moments [9,119].

3. COMPLEXES OF THE AZOLES WITH THE TETRAHALIDES OF GROUP IV ELEMENTS

The azole complexes with MX_4 (M = Sn, Ge, Ti, Zr, Hf, or Th; X = Cl, Br, or I) known hitherto are confined mainly to complexes of imidazole-containing systems [9,130-132]. Only in the case of tin tetrachloride have complexes been obtained also with benzo-2,1,3-thiadiazole (XVI, R = H) and its 5-methyl derivative (XVI, R = CH_3), [133,134] and germanium tetrachloride was found to form complexes with 3,5-dimethylpyrazole (XVII) and 2-methylbenzothiazole (XVIII). [9]



(XVI) (XVII) (XVIII) (XIX)

The azole complexes with Group IV metal tetrachlorides were synthesised by mixing in the cold the benzene or chloroform solutions of the ligands with MX_4 solutions in benzene (M = Sn, Ti, or Ge) [9,130,132] or ether (M = Zr, Hf, or Th). [9,131,132]

As for the coordination compounds of other oxygen- and nitrogen-containing ligands [9,104,132-135], the compositions of complexes of this type are fairly rigorously correlated with the properties of the MX_4. [9,132] Regardless of the reactant ratio and the bulk and basicity of the ligand, tin [9,130,133], zirconium [131], and hafnium tetrahalides [131] form coordination compounds of the type $MX_4.2L$. The complexes $MX_4.3L$ are most characteristic of germanium tetrachloride although (XVII) forms the complex $GeCl_4.L$

and imidazole even $GeCl_4.5L$.[9] Depending on the reactant ratio, titanium tetrachloride was found to form the coordination compounds $TiCl_4.2L$ and $TiCl_4.L$.[9,130,132] Thorium tetrachloride complexes of definite composition could be obtained only with ligands containing bulky substituents in the azole rings [for example (XIX) and the 1-(α-phenylethyl), 1-(α-naphthylmethyl), and diphenylmethyl derivatives resembling it][131]. Thorium tetrachloride forms with imidazole, benzimidazole, and their *CN*-alkyl(aryl) derivatives coordination compounds having the composition $ThCl_4.2L.n(C_2H_5)_2O$ in which n varies from 6 to 14 depending on the bulk of the ligand[132].

The study of the structure of the coordination compounds of MX_4 with azoles led to the conclusion that the only complex-formation centre in the imidazole ring is the pyridine-type nitrogen atom[130]. The conclusion was based on the increase of the stretching vibration frequencies in the imidazole ring (1550–1570 cm^{-1}) on complex formation and the similarity of a number of chemical and physical properties (spectroscopic behaviour on coordination) of imidazole-containing systems and pyridine[9,130]. Subsequently this test was widely used to demonstrate that coordination involves the pyridine-type nitrogen atom of the azole ligand[9,99,119-121,130-132,136-138].

It was also established that the stretching vibration shifts $\Delta\gamma$ of the imidazole ring on coordination interaction with MX_4 are correlated with the basicity of the ligand[9,130-132].

The structure of the complexes $MX_4.2L$ with azoles was not studied in detail owing to their extremely low solubility and ready hydrolysability. However, low-frequency vibration spectra show that the $SnCl_4$ and $TiCl_4$ complexes with benzimidazole as well as a number of other nitrogen-containing ligands[139] have the *cis*-octahedral configuration in the crystalline phase[9].

4. COMPLEXES OF AZOLES WITH GROUP V METALS

Complexes of azoles with niobium pentachloride[140,141] and niobium oxide trichloride[142-144] have been isolated on a preparative scale and partly investigated. The complexes of both niobium derivatives were obtained by the interaction of the ether compound of the pentachloride[140,141] or the chloride trioxide[142-144] with azoles in benzene solutions.

The composition of the coordination compound of $NbCl_5$ depends significantly on the basicity of the azoles and in many cases also on the reactant ratio and on the solvent. For azoles with a comparatively high basicity imidazole, benzimidazole, 2-methylbenzimidazole), the complexes $NbCl_5.nL$ with n = 1, 2, or 3 may be obtained for different reactant ratios[140,141]. As the basicity decreases (3,5-dimethylpyrazole and benzothiazole), the complexes $NbCl_5.L$ are formed[140,141]. When benzene is replaced by acetonitrile, the complex $NbCl_5.L.CH_3CN$ may be isolated[141].

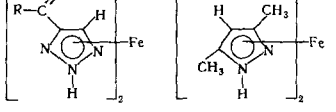
In contrast to the $NbCl_5$ complexes, the composition $NbOCl_3.L$ is most characteristic of the $NbOCl_3$ coordination compounds[142-144]. However, it is difficult to reach final conclusions concerning the dependence of the composition of the $NbOCl_3$ complexes with azoles on structural factors and conditions of synthesis owing to the narrow range of azole-containing systems which have been introduced into the reaction with niobium oxide trichloride[142-144].

The properties of the $NbCl_5$ and $NbOCl_3$ coordination compounds have been investigated by magnetochemical and infrared spectroscopic methods. It has been shown[140,141] that, when $NbCl_5$ interacts with azoles, niobium is not reduced to the quadrivalent state¶: all the complexes synthesised, except $NbCl_5.2L.CH_3CN$, are diamagnetic. On the other hand, the weak paramagnetism ($\mu_{eff} \simeq 0.7$ Bohr magneton) of the complex containing an acetonitrile molecule has been explained[141] by the coordination of CH_3CN to $NbCl_5$ (the complex $NbCl_5.CH_3CN$ is also weakly paramagnetic—μ_{eff} = 0.6 Bohr magneton).[148]

In view of the increase of the vibration frequencies of the azole ring in the complexes $NbCl_5.nL$[140,141] and $NbOCl_3.L$,[142-144] it was concluded that the coordinate bond involves the pyridine-type nitrogen atom of the azole ring. It was also established that the interaction of $NbOCl_3$ with azoles entails a decrease of absorption due to the NbO bond by 30–65 cm^{-1} (in the range 700–800 cm^{-1}). On this basis, it has been suggested that the frequency shifts of the bond stretching vibrations can serve as a kind of measure of the stability of the donor–acceptor bond between the ligand and niobium oxide trichloride[143,144].

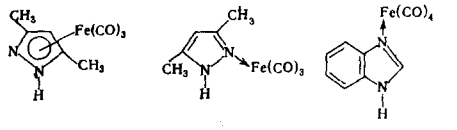
5. GROUP VI–VIII METAL CARBONYL COMPLEXES OF AZOLES

The synthesis and the study of the properties of the metal carbonyl complexes of azoles were undertaken mainly to investigate the possibility of the formation of π complexes in the azole series. On the basis of the available data concerning the successful synthesis of azoferrocene[149-152] and the similarity of a number of properties of azoles and pyrrole, Nesmeyanov et al.[33] allowed 4-butyryl(benzoyl)-1,2,3-triazoles and 3,5-dimethylpyrazole to react with iron nonacarbonyl. Elemental analysis, molecular weight measurements, and infrared spectra led the authors[33] to the hypothesis that the compounds (XX) and (XXI) obtained have the π-complex structure:



(XX), R = C_3H_7, C_6H_5 (XXI)

Later similar considerations were adduced concerning the structure (XXII) of azole complexes having the composition $LFe(CO)_3$[34-35] but σ-complex structures (XXIII) and (XXIV) were attributed to complexes of the type $LFe(CO)_4$ on the basis of mass spectrometric, infrared spectroscopic, and NMR studies[35,37]:

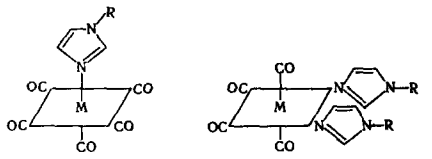


(XXII) (XXIII) (XXIV)

Complexes of a large group of azoles and their benzoanalogues with chromium, molybdenum, and tungsten hexacarbonyls were obtained by Beck et al.[41] and independently by Garnovskii and coworkers[46,48]. Elemental analysis [composition $LM(CO)_5$ or $L_2M(CO)_4$], infrared spectroscopy, dipole moment[46,48], and ^{14}N NMR measurements[41] suggested that all these compounds have the

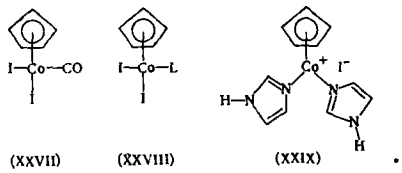
¶ Earlier it was stated that, when $NbCl_5$ interacts with nitrogen-containing organic compounds, paramagnetic coordination compounds of the type $NbCl_4.nL$ are formed[145-147].

σ-complex structure with an M ← N bond involving the pyridine-type nitrogen atom of the heterocyclic ring, for example (XXV) and (XXVI):



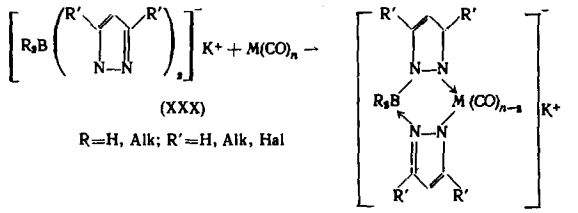
(XXV) (XXVI)

The reaction of cyclopentadienylcobalt di-iodide (XXVII) with imidazole, benzimidazole, indazole, and benzotriazole led to the synthesis of the complexes (XXVIII) and (XXIX) with a Co–N σ bond[153]:



(XXVII) (XXVIII) (XXIX)

Alkali metal polypyrazolylborates (XXX) react with molybdenum hexacarbonyl[154,155] and bromomanganese pentacarbonyl or dimanganese decacarbonyl[156] to form anions with a σ-linked metal carbonyl residue (XXXI):

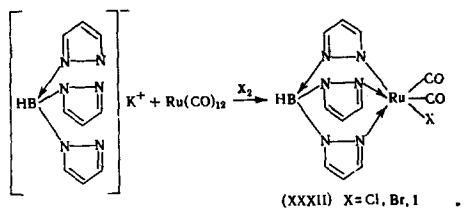


(XXX)

R=H, Alk; R′=H, Alk, Hal

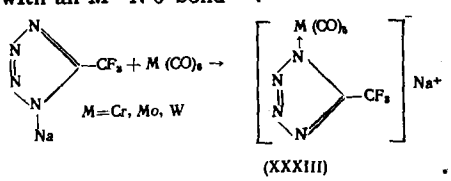
(XXXI)

The reaction of potassium tripyrazolylborate with $Ru_3(CO)_{12}$ in the presence of a halogen (Cl_2, Br_2, I_2) yields the metal carbonyl derivatives (XXXII) in which an Ru–N σ bond is formed[157]:



(XXXII) X=Cl, Br, I

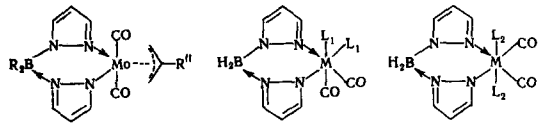
The anion (XXXIII), formed in the reaction of sodium 5-trifluoromethylpyrazolide with $M(CO)_6$, also has a structure with an M–N σ bond[166]:



M=Cr, Mo, W

(XXXIII)

The reactions of the above anions with unsaturated compounds[154] or phosphines (phosphites)[156] can yield the coordination compounds (XXXIV)–(XXXVI) respectively. In the case of phosphines, the ligands (L_1) occupy the *cis*-positions relative to one another [as in compound (XXXV)] and in the case of the phosphites (L_2) the complex has the *trans*-configuration (XXXVI):[156]



(XXXIV) (XXXV) (XXXVI)

Thus the data presented clearly demonstrate the preferential formation by azoles of σ and not π complexes even with powerful π acceptors such as metal carbonyls. We believe that the difficulty of obtaining π complexes in the series of azoles, in contrast to pyrrole[149–152,159,160] and other five-membered systems with one heteroatom[161,162], can be explained[9,48] by the combination in the azole molecule of a π-electron sextet with the unsaturated pyridine-type nitrogen atom, the electron-donating activity of which greatly exceeds that of the π-electron system†.

The study of the polar properties of complexes of the type $LM(CO)_5$ showed that the stability of the coordination compounds varies in parallel with the basicity of ligands of a similar type[9,48,48]: imidazole > benzimidazole > pyrazole > tetrazole. However, the stabilities of azole complexes containing oxygen or sulphur atoms in the heterocyclic ring (benzoxazole, benzothiazole) do not fit in the above sequence[9,46,48].

The considerable polarity (μ = 10 D) of azole complexes of the type $L_2M(CO)_4$ demonstrate their *cis*-octahedral configuration in solution[48,48]. According to infrared spectroscopic data, the complexes have the same structure in the crystalline phase too[41,48,48] (four bands in the range 1800–2000 cm^{-1}).

To conclude our discussion on coordination compounds with monodentate azoles, note that we have not discussed data for the coordination compounds of *N*-substituted tetrazoles, since a fairly complete review on this subject is available[72]. On the other hand, one must emphasise that, according to the latest X-ray diffraction data[165], the tetrazole ring can be coordinated not only via the $N_{(4)}$ atom[72] but also via the $N_{(3)}$ atom[166]. Together with the azole complexes discussed above, the coordination compounds of 2-methylbenzoselenazole[100], isothiazole[167,168], thia- and selena-diazoles[169–171], and also a number of azole solvates with the general formula $MX_2.2L.2H_2O$ (the latter have an octahedral configuration)[172] have also been investigated, albeit in less detail. Finally, in addition to the metals mentioned above, azole complexes of ruthenium[173,174], rhenium[175], and rhodium[171] have been synthesised.

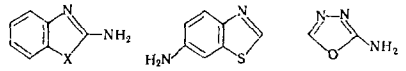
6. COMPLEXES OF AMBIDENT AZOLE-CONTAINING SYSTEMS

Azole ligands with several electron-donating atoms combined into a single conjugated system (ambident compounds[10,93]) are of considerable interest for the problem of competitive coordination in the chemistry of their complexes[9,10]; for this problem, it is useful to arrange the ligands of the azole series systematically in terms of the possible bonding atoms.

† The suggestion that π complexes are formed in the pyridine series[163] proved to be erroneous[164].

a. Azole-containing Ligands with Electron-donating Nitrogen Atoms

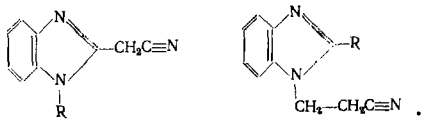
Amino-derivatives of azoles [(XXXVII)–(XXXIX)] containing two electron-donating nitrogen atoms hybridised in different ways are mainly monodentate ligands and form with transition metal salts [86,98,176-180] and the halides of Group I, [180] III, [9,119] IV, [9,132,181] and V [140-144] complexes in which the coordinate bond involves mainly the pyridine-type ring nitrogen atom:



(XXXVII) (XXXVIII) (XXXIX)

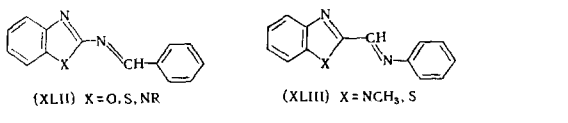
X = O, S, NR; R = H, Alk, Ar

Only in a few cases has it been claimed that the complex may be formed with participation of both electron-donating centres [9,140,141] and, in the case of compounds (XXXVII) [180] and (XXXIX), [178] with participation of the amino-nitrogen. In amino-derivatives of azoles, coordinating attack is directed to the nitrogen heteroatom with the highest π-electronic charge (the X atom and the amino-nitrogen are positively charged) [9,181]. Although this result, which follows from infrared spectroscopic [9,132,140-144] and ultraviolet spectroscopic [86,176,177,180] studies, conflicts with Pauling's postulate that the electron-donating capacity of nucleophilic atoms increases with the amount of p-character of the hybrid orbitals [182], it is consistent with data showing that the coordinate bond involves the electron-donating centre with the maximum negative potential [183] and hence with the maximum negative π-electronic charge [10,184]. Similarly the coordinate bond in the cyano-derivatives of the azole series (XL) and (XLI) involves the nitrogen atom of the heterocyclic ring [9,185]:



(XL) (XLI)

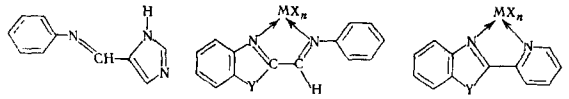
Similarly complexes are formed via the nitrogen atom with the maximum negative π-electronic charge in the series of azole-containing systems with equally hybridised nitrogen atoms: the anils (XLII) and (XLIII) via the azomethine nitrogen atom [9,10,181] and the azo-compounds (XLIV) [9,186] and formazans (XLV) [187,188] via the pyridine-type heterocyclic nitrogen atom:



(XLII) X = O, S, NR (XLIII) X = NCH$_3$, S

(XLIV) R = Alk, Ar, cyclo-C$_4$H$_8$ (XLV) X = O, S, NR$''$; R = CH$_3$; R$'$ = Alk, Het (XLVI) X = NH, S

At the same time, the ligands (XLIII), (XLIV), and (XLVI) [185,186,189-208] as well as (XLVII), [209] containing electron-donating nitrogen atoms in positions favouring the formation of cyclic structures, give rise to chelate complexes (XLVIII) and (XLIX):



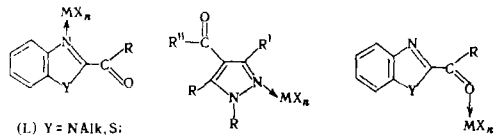
(XLVII) (XLVIII) (XLIX)

The composition and structure of complexes of ambident nitrogen-containing systems depend on the same factors as the complexes of monodentate azoles. 2-Aminobenzazoles (XXXVII) form mainly complexes of type $MX_2.2L$. [86,176,177] However, the coordination compounds of 2-aminobenzothiazole (XXXVII, X = S) with the composition $Co(ClO_4).3L$ may be isolated [176] and synthesis in a hydrochloric acid medium yields the complexes $MX_2.L$ (M = Cu, Co, or Hg). [179] Depending on the reactant ratio, 2-amino-1,3,4-oxadiazole (XXXIX) forms the coordination compounds $MX_2.nL$ (n = 2–6). [178] The type of polyhedra formed is determined by the electronic structure of the metal (the cobalt complexes are mainly tetrahedral [86,176,177]) but it depends also on the anion [86].

The bulky ligands (XLII)–(XLVI) tend to decrease the coordination number of the metal and to form mainly the complexes $MX_m.L$, [9] while the coordination compounds of bisazole systems (XLVI) give rise to planar or polymeric-octahedral structures [199,202,205].

b. Oxygen- and Sulphur-containing Derivatives of Azoles

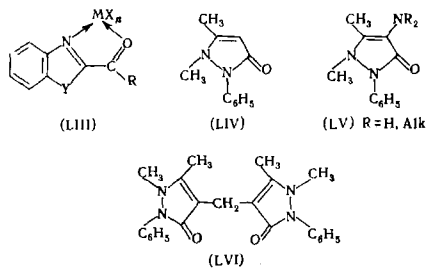
Infrared spectroscopic studies demonstrate fairly clearly that, in complexes of C-carbonyl derivatives of the azole series [(L) and (LI)], the coordinate bond involves mainly the nitrogen atom of the heterocyclic ring [9,119,210].



(L) Y = NAlk, S; R = H, Alk (LI) R = H, Alk (LII)

Only the "hardest" [10] Lewis acids $AlCl_3$ and $AlBr_3$ form complexes via the oxygen atom: (LII) and (LIII). [9,210]

Antipyrine (LIV) and its derivatives (LV) and (LVI) form two types of complexes depending on the conditions of synthesis: $MX_m.nL$ in neutral or weakly acid media [9,132,211-226] and ionic association complexes of the antipyrinium cation in acid solutions [212,223,226-230].

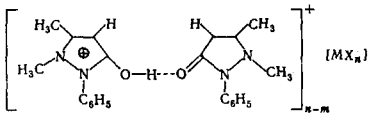


(LIII) (LIV) (LV) R = H, Alk

(LVI)

Regardless of the nature of MX_m, the formation of the complexes $MX_m.nL$ involves exclusively the exocyclic oxygen atom [9,132,211-230], which is consistent with the high

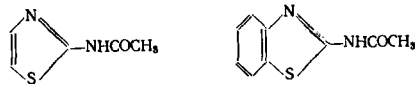
negative π-electronic charge of the oxygen atom [9,132,225,231,232]. In the ionic association complexes (LVII), the proton adds to the same electron-donating centre [226-230].



(LVII)

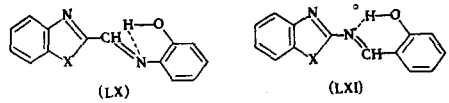
A cyclic structure with the metal coordinated to exocyclic oxygen and nitrogen atoms has been attributed [233-235] to 4-aminoantipyrine (LV, R = H) and its *N*-dimethylamino-derivative (LV, R = CH_3). Complexes of ligands of this type have an octahedral structure regardless of the metal and the anion [236].

2-Acetamidothiazole (LVIII) and its benzo-analogue (LIX) are ambident systems whose complexes with different MX_2 may be formed in three ways: (1) via the nitrogen atom in the thiazole ring ($CuCl_2$), (2) via the amide oxygen atom and the heterocyclic nitrogen atom (NiX_2, X = Cl, Br, or I; $CuBr_2$), and (3) via the amide and ring nitrogen atoms [CuX_2, X = NO_3 or ClO_4; $Ni(NO_3)_2$]. [237]

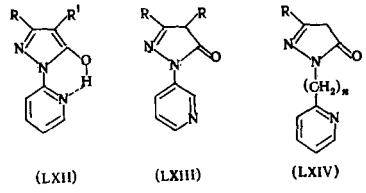


(LVIII) (LIX)

o-Hydroxyanils of the azole series (LX) and (LXI) [9,132,189] and the 5-hydroxy derivatives of 1-pyridylpyrazole (LXII)–(LXIV) [185,204] are unusual ambident nitrogen- and oxygen-containing ligands.



(LX) (LXI)

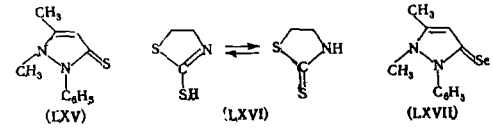


(LXII) (LXIII) (LXIV)

Compounds (LX)–(LXII) form complexes via the azomethine [compounds (LX) and (LXI)] [9,132,189] or pyridine-type nitrogen atoms [185,204]. However, for ligands with a preferential oxo-form [(LXIII) and (LXIV)], [9,185,204,238] the coordinate bond involves the oxygen atom of the carbonyl group [185,204].

There are comparatively few data concerning the nature of the polyhedral forms of these complexes. Antipyrine complexes of the type $CuCl_2.2L$ and $CuBr_2.2L$ are known to be pseudotetrahedral and the complexes $Cu(NO_3)_2.2L$ are planar or have a distorted octahedral structure [214]. The complex $Cu(ClO_4)_2.5L$ has a pentacoordinate copper atom [215] and the copper complexes with acetate or arenecarboxylate anions have tetragonally distorted octahedral structures [224]. The octahedral configuration is characteristic of antipyrine complexes of the type $M(ClO_4)_2.6L$. [239]

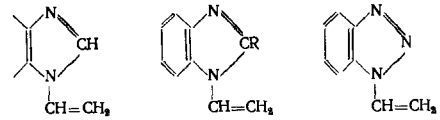
Thiopyrine (LXV) [217] and thiazolidenethione (LXVI) [240] must be classified as sulphur- and nitrogen-containing ambident systems.



(LXV) (LXVI) (LXVII)

In the coordination compounds of both ligands, the coordinate bond involves the exocyclic sulphur atom. Similarly, the coordination interaction [9] of selenapyrine (LXVII) involves the exocyclic selenium atom. The complexes of thiazolidine-2-thione (LXVI) have been investigated in fair detail [240]. Magnetic and spectroscopic (ultraviolet and infrared) studies established that the complexes $MX_2.2L$ are tetrahedral (M = Co, X = Cl, Br, or I; M = Ni; X = I) or octahedral (M = Ni, X = Cl or Br). [240]

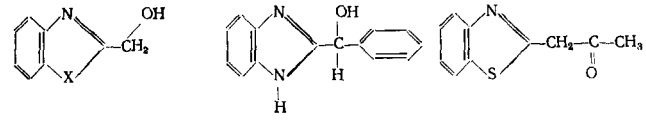
Apart from the ambident systems mentioned above, *N*-vinyl derivatives of azoles (LXVIII)–(LXX) have been used to form complexes with metal salts [137,138,241,242]:



(LXVIII) (LXIX) (LXX)

The study of the interaction of tin and nickel chlorides with the ligands (LXVIII)–(LXX) showed that in this case too the composition of the complexes depends on the reactant ratio and on the nature of the ligand and the solvent [241,242]. Infrared, ultraviolet, and NMR spectroscopic studies showed unambiguously that the coordinate bond involves the pyridine-type nitrogen atom of the azole ring. [137,138,241] A similar conclusion was reached concerning the structure of the cobalt complexes of *N*-vinylbenzimidazole and a number of its 2-alkyl(arylalkyl) derivatives (XIX). [242]

Together with the complexes of the amibdent systems, those of a number of azole ligands with isolated electron-donating centres have been obtained: 2-hydroxymethyl derivatives of benzimidazole (XXI) [68,81,243-247] and benzothiazole (LXXII), [26,96,248] 2-(α-hydroxybenzyl)benzimidazole (LXXIII), [249] and 2-acetonylbenzothiazole (LXXIV): [26]



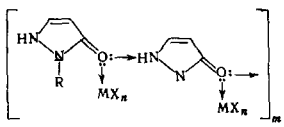
(LXXI) X=NH
(LXXII) X=S (LXXIII) (LXXIV)

The ligands (LXXI)–(LXXIV) are bidentate; the complexes are formed via the pyridine-type nitrogen atom of the azole ring and the hydroxyl oxygen, as a result of which they have a chelate structure with an octahedral configuration. Apparently the ligand (LXXIV) also occupies two coordination sites in the coordination compound [26]. However, in order to reach a final conclusion concerning the mode of its coordination, it is necessary to make a detailed infrared spectroscopic study of the stretching vibration frequencies of the carbonyl group on complex formation.

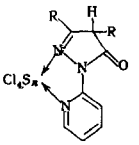
7. STABILISATION OF TAUTOMERS AND CONFORMERS OF AZOLE-CONTAINING COMPOUNDS AS A RESULT OF COMPLEX FORMATION

It is believed [250] that the formation of chelate complexes results in the stabilisation of specific tautomeric forms of the ligands (for example the enol and thiol forms in the metal chelates of acetylacetone [251] and its thio-analogues [252-254]). However, these examples of the stabilisation of one of the tautomeric forms as a result of complex formation are not altogether correct. In the coordinated ligand of a chelate complex, the bonds are known to be partly equivalent (acetylacetonates) and therefore it is difficult to speak of the stabilisation of a particular tautomeric form as a result of the formation of the chelate. On the other hand, it has been shown [9,255] that the hypothesis of the stabilisation of one of the tautomeric forms of the ligand as a result of complex formation is valid for molecular complexes in which the ligand [bonding] system is fully retained.

The infrared spectra of the complexes of pyrazolones as well as of the coordination compounds of antipyrine (LIV) show bands due to the NH group (2400–3300 cm^{-1}) and the protonated antipyrine ring (1550–1600 cm^{-1}). Moreover, frequencies characteristic of the complexes of MX_n with 3,4,4-trimethylpyrazolone-5-one do not occur in the region of 1700 cm^{-1}. These data suggest that in the pyrazolone complexes the antipyrine structure is stabilised and the complexes have the structure of coordination polymers (LXXV):



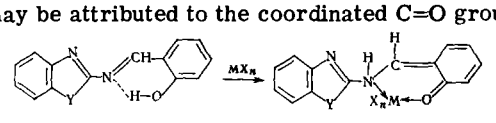
(LXXV)



(LXXVI) R = H, Alk

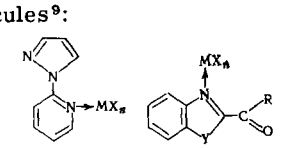
In the complexes of 1-(α-pyridyl)pyrazolones (LXII), the pyrazolone tautomeric form (LXXVI) is stabilised: the infrared spectra of the complex of (LXII) with $SnCl_4$ show absorption due to the free carbonyl group (1710 to 1715 cm^{-1}). [204]

A study of the infrared spectra of complexes of MX_n with o-hydroxyanils of the benzazole series led to the view [9] that the quinonoid form (LXXVII), which is "uncharacteristic" of o-hydroxyazomethines, is stabilised by complex formation: at 1650 cm^{-1} a band was observed, which may be attributed to the coordinated C=O group:



(LXXVII)

It has been established that not only tautomers but also conformers of compounds of the azole series may be stabilised by complex formation [9]. This may involve the retention or an alteration of the configuration of the ligand compared with the form of the non-coordinated azole molecule. In their complexes with MX_n, 1-(α-pyridyl)-pyrazoles [204] and 2-formylbenzazoles [210] retain the *S-trans*-configurations (LXXVIII) and (LXXIX) characteristic of free azole molecules [9]:



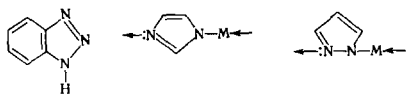
(LXXVIII) (LXXIX)

Only the complexes of carbonylazoles with AlX_3 (X = Cl or Br) form cyclic structures (LIII) in which the ligands assume the *S-cis*-form [9]. A similar conversion of the *S-trans-trans*-form into the *S-cis-trans*-configuration (XLVIII) is observed when anils of 2-formylbenzazoles (XLIII) react with MX_n. [9,189] It has been concluded [9] that the stabilisation of one of the conformers need not necessarily be due solely to the structure of the ligand system as is usually postulated for a whole series of bisheterocyclic systems (bipyridyl): the properties of the complex-forming agent (MX_n) play an extremely important role in this process.

III. *N*-METAL AND *N*-ELEMENT DERIVATIVES OF AZOLES

Azoles with an unsubstituted NH-group exhibit acid properties on interaction with metals. The acidity constants of tetrazole and its derivatives ($pK_b = 5$), which are the most acid of the azoles, are close to those of acetic acid ($pK_b = 4.76$), while imidazole, which is least acidic, has $pK_b = 14.52$. Despite the comparatively low pK_b values of azoles, *N*-metal-substituted derivatives of imidazole [13,16,49,50,122,172,256-263], pyrazole [113,264,265], triazoles [261,266-268], tetrazole [269-277], benzimidazole [4,57,278], and benzotriazole (LXXX) [261,279-285] are now known.

In contrast to the molecular complexes discussed in section II, *N*-metal-substituted azoles contain covalent M–N σ bonds and electron-donating (sp^2-hybridised nitrogen) and electron-accepting (metal atom) centres not involved in coordination interaction [compounds (LXXXI) and (LXXXII)]:



(LXXX) (LXXXI) (LXXXII)

Therefore molecules of types (LXXXI) and (LXXXII) tend to undergo self-association and to form polymeric structures [9,50,125,258-262,270]. Metal-containing polymers of the azole series have anomalous magnetic properties (the μ_{eff} are lower than the spin-only values), which is attributed to a metal–metal exchange interaction via the π-electron system of the azole rings [4,9,261,262,268] or to a metal–metal bond [50].

The study of the magnetic properties [4,50,57,258,259] and reflection spectra [4,50,57] leads to the conclusion that the type of polyhedra formed in the crystalline phase by *N*-metal-substituted azoles depends primarily on the nature of the metal [50]. Copper complexes of imidazole and benzimidazole [57] have distorted tetrahedral (almost planar) structures, cobalt and zinc coordination compounds have tetrahedral structures regardless of the type of ligand [4,49,50,113], and nickel complexes have predominantly planar structures [16,50,258,259].

The capacity of azoles with an unsubstituted NH group to form *N*-element-substituted compounds was observed in the 1960's by several independent groups of investigators [9]. Birkofer developed a method for the synthesis of *N*-silyl derivatives of azoles [286,287], which proved to be exceptionally reactive in the synthesis of numerous *N*-substituted azole derivatives [286-291]. Systematic studies on *N*-trialkylmetal derivatives of azole-containing systems have been made by Van der Kerk and coworkers [292-305].

The development of the chemistry of pyrazole derivatives of boron is associated mainly with studies by

Trofimenko [154,155,265,302-306]. Other investigations in this field have also been made [125,307-311].

The choice of conditions for the synthesis of *N*-element-substituted derivatives depends on the acidity of the NH group of azoles, the reactivity of the metallating agents, and the resistance of the complexes obtained to hydrolysis. Tetrazole reacts with trimethylsilane under exceptionally mild conditions (benzene, 10°C), [287] while the synthesis of *N*-trimethylsilyl-substituted derivatives of other azoles requires heating of the azole system with hexamethyldisilazane for many hours [286]. The trimethyl derivatives of the majority of Group III elements react even with imidazole, the least acid compound of this series, in benzene or hexane in the cold [9,122], but BR_3 derivatives react only under comparatively severe conditions [9,119,302,305].

The majority of *N*-metal derivatives of the azole series are readily hydrolysed, but tin-, [297,299-301] germanium-, [296] and lead-substituted [298] compounds are comparatively stable. Therefore *N*-trimethylmetal derivatives can be obtained from the oxides [297] and hydroxides [293,298,308] of the corresponding elements:

$$(R_3M)_2O + 2HN\!\!\rangle \rightarrow 2R_3M{-}N\!\!\rangle + H_2O\ ,$$

$$R_3MOH + HN\!\!\rangle \rightarrow R_3M{-}N\!\!\rangle + H_2O\ .$$

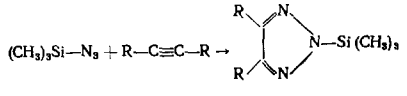
N-Element-substituted derivatives are obtained with the aid of the above reactions for a number of azoles and benzazoles and also purines [308]. *N*-Phenylmercury derivatives of imidazole, benzimidazole [312], and pyrazole [313] systems are obtained in the same way.

N-Metal carbonyl derivatives of the azole series are successfully synthesised by methods based on the interaction of alkali metal salts of azoles with metal carbonyl halides [154] or their π-cyclopentadienyl derivatives [34,35,45,314,315]:

$$\rangle N{-}M + X\,(CO)_2FeC_5H_5{\cdot}\pi \rightarrow \rangle N{-}Fe\,(CO)_2C_5H_5{\cdot}\pi\ ,$$

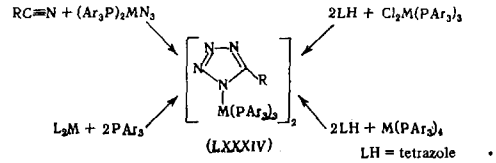
where M = Na or K, X = Cl, Br, or I, and $\rangle N$ is a heterocyclic group. This reaction was first widely employed by Seel to prepared a series of σ-complexes of azoles with π-cyclopentadienyliron dicarbonyl [45,314]. Subsequently the analogous benzotriazole derivatives [34,35,315] and rhodium dicarbonyl complexes of pyrazoles [154] were synthesised in the same way. The reaction serves as a basis for the synthesis of rhodium and palladium complexes of pyrazole and its derivatives linked by π bonds to olefins [154,155].

N-Element-substituted derivatives of azoles can be obtained not only directly from the heterocycles but also by an indirect method. Thus Birkofer [287,289] employed the 1,3-cycloaddition of trimethylsilyl azides to synthesise *N*-trimethylsilyl derivatives of 1,2,3-triazoles (LXXXIII):



(LXXXIII)

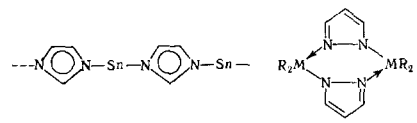
The synthesis of bis[tetrazolyltris(triphenylphosphine)-metal] complexes (LXXXIV) [8,90] in which the metal is copper, palladium, platinum, and ruthenium has been achieved on the same basis although other methods for the synthesis of complexes of this class from tetrazole or its *N*-metal derivatives have been developed [277,316]:



(LXXXIV) LH = tetrazole .

N-Element-substituted derivatives of azoles, like the *N*-metal-substituted derivatives discussed above, are mainly coordination-saturated oligomers or polymers [296-301,312,317]. Comparative viscometric studies showed that organotin polymers contain association complexes with much higher molecular weights than the organogermanium polymers [296].

The structure of *N*-element-substituted derivatives of azoles has so far been very little investigated. It has been postulated, albeit without insufficient justification, that trialkyltin derivatives of imidazoles have a linear coordination-saturated structure (LXXXV) with a pentacoordinate tin atom and equivalent bonds [297,317]:

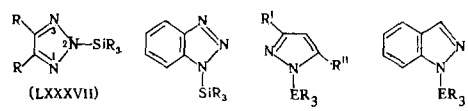


(LXXXV) (LXXXVI) M = B, Al .

According to NMR spectroscopic data, *N*-phenylmercury derivatives of 4,5-dichloro-2-methylimidazole have a similar configuration [312], *N*-dialkylmetal derivatives of azoles [9,119,122,265,303,306], *N*-trimethylsilylazoles [287,291], and *N*-phenylmercury derivatives of imidazole [312] and pyrazole [313] have been most thoroughly investigated among compounds of this class.

Cryoscopic (ebullioscopic) studies, NMR spectroscopy, and determinations of dipole moments showed [9,119,122] that the type of oligomers of the alkyl derivatives of Group III elements under consideration depends on the nature of the ligand (the distribution of nitrogen atoms in the heterocyclic ring) and on the properties of the ER_n substituent, where E is an element and R an organic group. *N*-Trialkyl-boron- [155,265,303] and -aluminium-substituted [9,122] pyrazoles are highly symmetrical dimers (LXXXVI), while the complexes of imidazole, benzimidazole, and tetrahydrobenzimidazole with the same substituents are probably linear polymers [9,119,122]. *N*-Dimethyl-gallium and -indium derivatives form cyclic tetramers or hexamers in solution regardless of the type of azole [9,122].

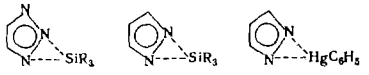
N-Trimethylsilyl(germyl)-substituted triazoles [289], pyrazoles [291,309], and indazoles [309] have been investigated mainly in connection with the determination of the position of the ER_n substituent in the azole ring [289,309] and of the elementotropic mobility of the ER_3 group [289,291]. Measurements of the dipole moments of a series of $NSiR_3$-substituted 1,2,3-triazoles showed that these complexes have the structure (LXXXVII) with the substituent in the 2-position of the triazole ring [289]. However, the analogous benzotriazole derivative (LXXXVII) contains the SiR_3 substituents in the 1-position [289]:



(LXXXVII) R = CH_3 (LXXXVIII) (LXXXIX) (XC) .

Elguero et al.[309] determined from NMR spectroscopic data the position of the ER_3 substituent (E = Si or Ge; R = CH_3 or C_2H_5) in pyrazoles (LXXXIX) and in indazole (XC).

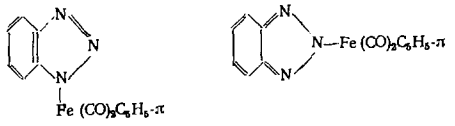
In 1966 Birkofer[289] suggested that the SiR_3 group may migrate readily between the nitrogen atoms of the triazole ring (XCI):



(XCI) (XCII) (XCIII)

Subsequently this elementotropic mobility of the *N*-substituent was observed for methylsilyl derivatives of pyrazole (XCII)[304] and was demonstrated almost unambiguously in a series of *N*-phenylmercury derivatives of the same heterocycle (XCIII).[313]

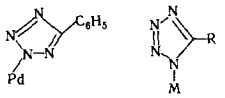
The situation is different with the coordination-saturated *N*-substituted derivative of benzotriazole containing a substituent with a relatively low mobility—π-cyclopentadienyliron carbonyl[315]. In this case, it is possible to isolate two isomers in which the substituent is linked to different nitrogen atoms of the triazole ring [(XCIV) and (XCV)].[315]



(XCIV) (XCV)

Thus even a limited number of examples demonstrate that not only is it possible to observe elementotropism in azole *N*-substituted derivatives of the elements but also one can isolate stable isomers involving different positions of the substituent relative to the nitrogen atoms of the heterocyclic ring. Nesmeyanov et al.[315] noted that the formation of similar isomers could probably be expected also for *N*-metal-substituted benzotriazole systems. We believe that, when the substituents and temperature conditions are suitably chosen, elementotropism may be observed or stable isomers isolated also for other *N*-element- and possibly *N*-metal-substituted triazole and tetrazole systems.

In this connection it is interesting to note that X-ray diffraction studies led to the discovery of a 2-palladium-substituted 5-phenyltetrazole derivative (XCVI),[277] while 1-metal-substituted structures (XCVII) have been postulated for other metals[269-277]:



(XCVI) (XCVII)

In conclusion we may note that the reaction of alkali metal borohydrides with pyrazole yielded polypyrazolylborates[154,302,303,305], which are exceptionally interesting ligands for the synthesis of metal chelates[165,265] and π complexes[154-157,306].

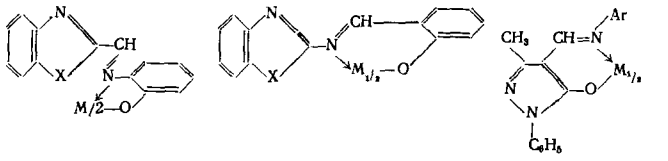
IV. CHELATE COMPLEXES IN THE AZOLE SERIES

Numerous chelate complexes synthesised from azole ligands‡ and containing chelate groups of the types MO_2N_2, MS_2N_2, MSe_2N_2, and MN_4, which are of greatest importance for coordination chemistry, are now known. In considering the methods of synthesis, the physicochemical properties, and the structures of complexes of this class, it is useful to arrange them systematically in terms of different types of coordination units.

‡ Azole-containing systems with chelating groups occupy an outstanding place among analytical reagents, metallochromic indicators, and extractants[6-9,318-338].

1. METAL CHELATES WITH AN MO_2N_2 COORDINATION UNIT

The hydroxyazomethines (LX)[9,339,340] and (LXI)[9,339] and 4-aminomethylene derivatives of pyrazolones[9] interact with bivalent metals salts to form chelates with five-membered [compounds (XCVIII)][9,340-344] and six-membered [compounds (XCIX) and (C)][9,189,344,345] metal-containing rings:



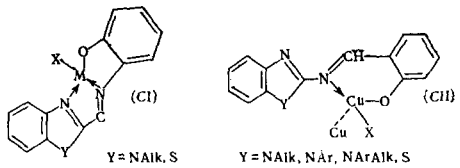
(XCVIII) (XCIX) (C)

The most typical composition of the chelates is ML_2, where LH are the ligands (XCVIII)–(C).[9,341-345] However, the anils (XCIX) form the complexes $ML.COOCH_3$ with copper(II), manganese(II), cadmium(II), lead(II), and $U^{II}O_2$.[341-344] Copper complexes of a similar type were obtained also for the azomethines (XCIX).[9,189] On the other hand, zinc and cadmium complexes with the composition ML_2 can be synthesised by refluxing the *o*-aminophenoxides of the above metals and the corresponding 2-formylbenzazoles in dioxan[344].

The chelate structure of the above complexes was established by comparing the infrared spectra of the coordination compound and the ligand: the hydrogen atoms of the hydroxy-group are found to be substituted [the bands corresponding to the OH stretching vibrations in the range 3400–3450 cm^{-1} for compound (LX)[339] and 3000–4000 cm^{-1} for compound (LXI)[9,189]] and the stretching vibration frequencies of the azomethine linkage increase[342,344]. Magnetic measurements showed that, as for the chelates of aromatic azomethines with a five-membered metal-containing ring[104,346-351], the complexes of the *o*-hydroxyanils (LX) have a tetrahedral or polymeric-octahedral configuration in the crystalline phase[343,344]. In contrast to the chelates of aromatic *o*-hydroxyazomethines with a six-membered metal chelate unit[104,352], coordination compounds of types (XCIX) and (C) have a polymeric-octahedral structure in the solid phase and a tetrahedral structure in solution regardless of the complex-forming metal[9,344,345]. These differences were explained[9,344] by the additional coordination of the metal to the pyridine-type nitrogen atom of the azole ring, which leads to an increase of the number of binding sites of the ligand actually employed (octahedron) or stabilises the tetrahedral configuration in solution.

Copper chelates with the acetate anion have unusual magnetic properties: while the chelates of the azomethine (XCVIII) have effective magnetic moments (μeff) corresponding to one unpaired electron (1.8–1.9 Bohr magnetons) the complexes of the *o*-hydroxyanils (XCIV) and (C) have the anomalous values μeff = 1.47–1.62 Bohr magnetons[9,344]. This result is attributed[9,344,351] to the formation in the first case of the coordination-saturated structure (CI) and metal–metal exchange interaction, while in the second

case the structure (CII) is believed to be formed via a Cu–Cu linkage or an acetate bridge [353,354]:

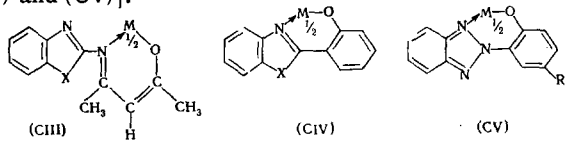


(CI) (CII)

Y = NAlk, S Y = NAlk, NAr, NArAlk, S

X = $OCOCH_3$

The six-membered metal chelate unit MN_2O_2 is also formed in the chelates of β-aminovinylketones [compounds (CIII)] [9] and 2-(*o*-hydroxyphenyl)benzazoles [compounds (CIV) and (CV)]. [9,14,191,355–361]

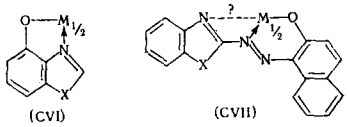


(CIII) (CIV) (CV)

X = S; NC_2H_5 X = O, S, NH R = H, CH_3; n-C_4H_9 .

The synthesis of the chelates (CIII) was achieved by the reaction of the metal acetylacetonates with 2-aminobenzazoles [9] and compounds (CIV) and (CV) were obtained by direct interaction of metal salts (the acetates are best) [358,359] with 2-(*o*-hydroxyphenyl)benzazoles. In the crystalline phase, all these complexes apparently have a polymeric-octahedral structure [9,361]. The initial hypothesis of a tetrahedral configuration of the metal chelates (CIV) [359] was shown to be erroneous by X-ray diffraction studies [361] §: in the copper and palladium complexes the metal is located in the plane of the coordination unit, but, as a result of the intermolecular (axial) coordination of copper(II) or palladium(II) to the oxygen atom of an adjacent metal-containing ring, a polymeric-octahedral configuration is produced [361].

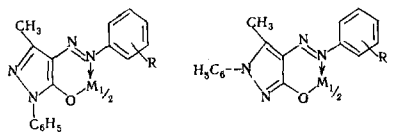
The 4-hydroxybenzazole complexes (CVI) were investigated [363–366] only in order to compare their stability with that of the chelates of the very important analytical reagent 8-hydroxyquinoline. It was found that, with the exception of the zinc complexes, the stability of the chelates fits the Irving–Williams series and is lower than that of the 8-hydroxyquinoline complexes [363–366]:



(CVI) (CVII)

X = O, S, NH X = O, S, NR:
R = H, Alk .

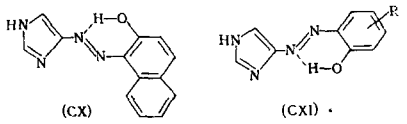
Hydroxyazo-derivatives of benzazoles (CVII) [9,341,367] and pyrazolones [compounds (CVIII) and CIX)] [368–370] yielded chelates with a six-membered metal chelate unit MO_2N_2, which in the crystalline phase has mainly an octahedral structure [9,370,371,373] and in solution mainly a tetrahedral structure [9,373].



(CVIII) R = H: *o*, *m*, *p*-CH_3; OCH_3; SCH_3; Hal; NO_2 (CIX) .

The tetrahedral configuration of chelates of type (CVII) precludes the intramolecular coordination of the metal to the nitrogen atom of the heterocyclic ring [314,367] and was adopted *a priori* for complexes of pyridylazonaphthol and related heterocyclic compounds [374–377], including benzothiazolylazonaphthol [375,378].

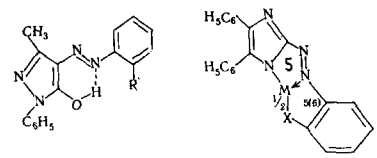
Snavely and coworkers have carried systematic determinations of the stability constants of chelates of types (CVIII) and (CIX). [369,370,372,378] The studies of Yamayichi et al. [379] of the properties of *o*-(4-hydroxyaryl)azoimidazole complexes (CX) and (CXI) had the same aim¶. However, thermodynamic data were not obtained in any of these investigations and therefore the conclusions arrived at must be treated with a certain amount of caution:



(CX) (CXI)

R = *p*-OCH_3, *m*-$N(CH_3)_2$.

Schetty's studies on the structures of the chromium chelate complexes of the tridentate azopyrazolone systems of type (CXII) need not be specially considered, since they have been reviewed by the author himself [380]:

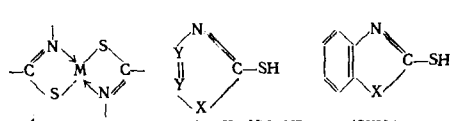


(CXII): R = OH, COOH (CXIII): X = O^-, COO^- .

We shall mention only that, after the publication of his review, a number of reports by the same author appeared, in which are described stereoisomeric chromium chelates of azopyrazolone derivatives (CXII, R = COOH) [381] and also complexes of 2-(*o*-hydroxyphenyl)-4,5-diphenylimidazoles with 5/5- or 5/6-metal-containing rings [382].

2. CHELATES OF TYPES MS_2N_2 AND MSe_2N_2

Complexes of 2-mercaptoazoles (CXV) [383–385] and 2-mercaptobenzazoles (CXVI) [386–393] with a five-membered metal-containing ring of type MN_2S_2 [structure (CXIV)] have been investigated. The majority of the studies were directed towards the analytical applications of compounds (CXV) and (CXVI) for a quantitative determination of platinum group metals [338,384–386,389,394,395].



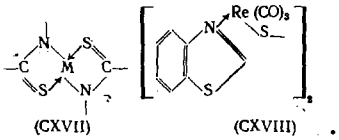
(CXIV) (CXV) X=NH, NR; Y=CR; Y=N (CXVI) X=NH, S .

However, in some of the investigations data have been obtained for the structures of the chelates synthesised from mercaptoazoles [387,392,393,396]. It is believed [392] that

§ In constructing a model of the metal chelate unit, Verkhovedova et al. [359] employed the usual [362] M–O bond lengths of 1.8–1.9 Å. However, in chelates of type (CIV) they actually exceed 2 Å.

¶ They described [379] the metal chelate (CXI–LH) with the composition LCuBr, in which according to infrared spectroscopy the hydrogen atom of the OH group and not the NH group is substituted by the metal.

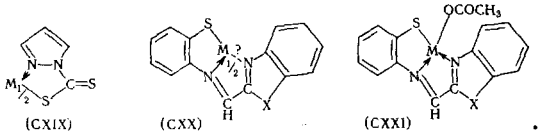
the bis(azathio)chelate unit (CXIV) is most probably formed rather than the thione configuration (CXVII):



(CXVII) (CXVIII)

The chelates of 2-mercapto-1-phenyltetrazoles (CXV, X = NH, Y = N) of type RuL_3 have an octahedral structure and those of types PtL_2 and $(RhL_2)_2$ have a planar structure [390]. The same derivatives of tetrazole with $Rh(PAr_3)_3Cl$ form mixed triphenylphosphine complexes of rhodium in which an Rh–S bond (300 cm^{-1}) and a metal chelate unit with a square planar configuration were found [396]. The dimeric octahedral complex (CXVIII) of 2-mercaptobenzothiazole with rhenium tricarbonyl is of undoubted interest [397].

A five-membered metal chelate unit of the type under consideration is formed in 1-pyrazolyldithiocarboxylates (CXIX) [398] and in the chelates of *o*-mercaptoanils of 2-formylbenzazoles [compounds (CXX) and (CXXI)]. [9,343,344,399]

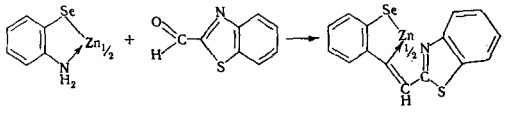


(CXIX) (CXX) (CXXI)

X = NCH_3, S

The complexes (CXX) and (CXXI) were shown to be metal chelates by infrared spectroscopy [9,343,399]. Magnetochemical studies make it possible to ascribe to the chelates (CXX) a polymeric-octahedral or tetrahedral configuration in the crystalline phase [9,343,399]. Intramolecular coordination of the metal to the nitrogen atom of the heterocyclic ring appears to be very probable in the complexes (CXXI), which have a normal magnetic moment [399].

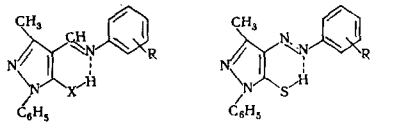
Recently an azomethine complex (CXXII) of the azole series containing a five-membered metal chelate unit with nitrogen and selenium atoms was synthesised [9,400]:



(CXXII)

As was to be expected [104], the zinc complex (CXXII) was found to have a tetrahedral structure in solution [400]. On the other hand, the pathways followed in the synthesis of this chelate with transition metals are still obscure†.

4-Phenylaminomethylene derivatives of thio- and selenopyrazol-5-one (CXXIII) [402] form chelates containing the six-membered coordination units MN_2S_2 [9,345,407] and MN_2Se_2, [9] which are rarely encountered with aromatic ligands [403–406]:



(CXXIII): R = H, *o*, *m*, *p*-CH_3, Hal, NO_2, OCH_3, $N(CH_3)_2$; X = S, Se

(CXXIV): R = H, *o*, *m*, *p*-CH_3, Hal, NO_2, OCH_3, SCH_3, $N(CH_3)_2$

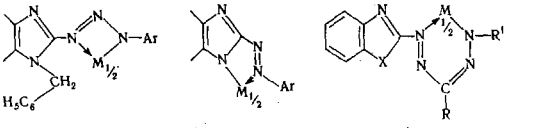
† Selenium-containing azomethines are unstable. On the other hand, a reaction similar to that indicated above proceeds only with seleno- and thio-phenoxides of non-transition metals [400,401].

The nickel complexes of the ligands (CXXIII) have unusual magnetic properties in the crystalline phase: in contrast to the mainly diamagnetic (planar) metal chelates containing nitrogen and sulphur atoms in the coordination unit [362,408,409], these chelate complexes have intermediate effective magnetic moments varying in the range 1.3–1.8 Bohr magnetons [9,345,407]. This result is attributed to the formation in the solid phase of a mixture of square planar (diamagnetic) and polymeric-octahedral (paramagnetic) forms [345,407]. On the other hand, in solution the nickel, cobalt, and zinc chelates of (CXXIII) are tetrahedral [9,345,407] according to their dipole (Ni^{2+}, Co^{2+}, Zn^{2+}) and magnetic (Ni^{2+}, Co^{2+}) moments. The cobalt and zinc chelates apparently have the same configuration in the crystalline phase [9,345]. The nickel‡ metal chelates of thioazopyrazolones (CXXIV), synthesised for the first time by Snavely [368,369,410,411], have the same properties in the solid phase [373,410] as their azomethine analogues (CXXIII). However, in solution the chelates (CXXIV) assume the diamagnetic and polar ($\mu = 3$ D) tetragonal-pyramidal configuration with the metal atom raised above the plane of the metal-containing ring [373,412].

3. CHELATES WITH MN_4 UNITS

In his review, Hennig [207] described fairly completely the studies on chelates based on ligands with an acid NH group, including those of the azole series with an MN_4 coordination unit. Therefore we shall consider only some of the fundamental characteristics introduced by the azole moiety into the configuration of the complexes in which the metal is linked to the nitrogen atoms.

In contrast to the usually planar chelates of aromatic compounds with an MN_4 coordination unit [362,408,409], the analogous metal chelates of azole-containing systems have in the crystalline phase mainly a polymeric-octahedral structure and in solution a tetrahedral structure. This difference between the configurations of the metal chelate units was observed in a study of the magnetic and polar properties of the chelates of the azole series with four-membered [the triazene complexes [9,413] (CXXV)], five-membered [complexes of azo-compounds [9,186,414–416] (CXXVI)], and six-membered [complexes of formazans [9,28,132,416–429] (CXXVII)] metal-containing rings.



(CXXV): Ar = C_6H_4X; X = H, *p*-Alk, *p*-Cl

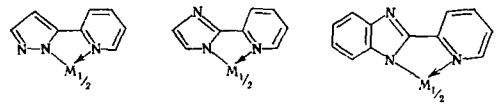
(CXXVI): Ar = C_6H_5, $C_6H_4CH_3$

(CXXVII): R = Alk, Ar; R' = Ar, Het

There is no doubt that the formation of polymeric-octahedral structures in the crystalline phase can be accounted for by the coordination of the metal to the nitrogen atom of the azole ring of an adjacent molecule (the monomeric units of such chelates are coordination-unsaturated) [9,418,422,424,425]. The only study in which intramolecular coordination of the metal to the sulphur atom of the thiazole ring in the nickel and cobalt complexes of *N*-thiazolylformazan [28] was postulated does not withstand criticism, since the above heteroatom virtually lacks electron-donating properties (see above). On the

‡ The chelates of thioazopyrazolones with other metals have been described and their stabilities have been determined [410,411].

other hand, planar polyhedra are encountered among chelates of the azole series with MN_4 metal chelate [207]. The latter include the nickel complexes (CXXVII) of pyridylpyrazoles, the planar structure of which has been demonstrated not only by magnetochemical [430] but also by X-ray diffraction [431] studies:



(CXXVIII) (CXXIX) (CXXX)

Possibly the above anomaly is associated with the comparatively low basicity of pyrazole. However, final conclusions will become possible only after detailed physicochemical and X-ray diffraction studies of the chelates of 2-pyridylimidazole (CXXIX) and its benzo-analogue (CXXX). [207,432]

ADDENDUM

During the preparation of the manuscript for the press, new data were published on the synthesis and structure of molecular complexes of azoles with transition metals [433-459] and complexes of polypyrazolyl borate ligands [460-462]§. Competitive coordination in the following ambident azole systems was considered: benzothiazole [445], benzoselenazole [457], *N*-vinylimidazole [439,440], 2-aminobenzazoles [463], pyridylmethylene-2-aminobenzothiazole [464], oligoheterocycles [465-470], and dinuclear copper complexes of 2-formylbenzimidazole aldoximes [471]. The structures and magnetic properties of complexes of the antipyrine series [472-483] and of acetamidothiazole [484] have been investigated.

Studies have been made on the physicochemical properties of *N*-metal-substituted 5-chloro- and 5-methoxyphenyltetrazoles [485], and 1-borylimidazole [486] and on the possible synthetic applications of silver and chloromercury salts of benzotriazole [487].

New metal chelates of *o*-hydroxyazo- [488] and *o*-hydroxyazomethine [489] derivatives of isoxazoles have been obtained. An electrochemical method has been developed [490] for the synthesis of chelates of types (XCVIII), (XCIX), (CIV), and (CV). Chelate complexes of copper(I) with 2-mercaptobenzothiazole [491] and of lanthanides with tetrazole-5-thione [492] have been synthesised.

Comparison of the properties of the chelates obtained [489,493] from pyrazole [(compounds (CXXIII)] [402] and pyrrole [494] mercaptoaldimines led to the conclusion that the heterocyclic moiety promotes a tetrahedral structure of the complexes with an MS_2N_2 coordination unit not only in solution [9,345,407] but also in the crystalline phase [489,493].

The ESR spectra of the copper complex (CXXVIII) of pyridylpyrazole have been investigated [495]. There has been a growth of interest in *C*-metal- and *C*-element-substituted derivatives of azoles [496-506]. *C*-Metal-substituted azoles have a polymeric-octahedral structure [496].

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§ See also the Editor's comments in Ref. 155.

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The State University,
Rostov-on-Don

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Electrochemical Oxidation of Carbon Monoxide in Aqueous Solutions

E.I.Konnik

The advances achieved recently in the electrochemical oxidation of carbon monoxide, which is a comparatively cheap fuel for electrochemical generators (fuel cells), are considered and the problems of the further improvement of the electrochemical oxidation of carbon monoxide are analysed. The electrochemical methods for the analysis of carbon monoxide, which are important for industry, medicine, and scientific research, are reviewed.
The bibliography includes 32 references.

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1. INTRODUCTION

The electrochemical oxidation of carbon monoxide has been the subject of study for a long time. Together with the hydrogen and hydrazine electrodes, the carbon monoxide electrode as well as electrodes comprising hydrocarbons and other organic compounds as reducing agents are of great interest as negative electrodes in current sources and in other fields of applied electrochemistry.

However, whereas the improvement of the hydrogen electrode, by K.Kordesch, F.T.Bacon, E.Justi and coworkers, R.Kh.Burshtein and coworkers, and others, has led to a considerable increase of the current generated by porous catalytic hydrogen electrodes, the improvement of the carbon monoxide electrode has been less satisfactory.

The reversible thermodynamic potential of carbon monoxide is much more negative than that of the hydrogen electrode, particularly in 5 M KOH where it is -1580 mV at 25°C relative to the saturated calomel electrode, i.e. more negative by 450 mV than the reversible hydrogen electrode in the same solution (Justi et al.[1], p. 244). The e.m.f. of a system comprising this electrode and a reversible oxygen electrode should be 1680 mV under these conditions. However, the steady-state potential of the carbon monoxide electrode attainable at present is between only -1210 and -1230 mV.

The use of the carbon monoxide electrode in current sources appeared unpromising until recently. The rate of electrochemical oxidation of carbon monoxide on smooth metal electrodes was so low that the current generated at a moderate polarisation amounted to a few microamperes per cm^2 of the true surface. This caused workers in the 1940s and 1950s to attempt to use the carbon monoxide electrode in current sources at 700 to 900°C.[2,3] Moreover, the life of such a cell did not exceed several days and the current density at an acceptable polarisation was a few mA cm^{-2}; as shown below, the use of high temperatures is thermodynamically unfavourable.

2. THERMODYNAMIC PRINCIPLES AND HISTORY OF THE ELECTROCHEMICAL OXIDATION OF CARBON MONOXIDE

In studies on the thermodynamics of the electrochemical oxidation of carbon monoxide, one uses as the cathodic process the electrochemical reduction of oxygen, the characteristics of which at catalyst electrodes made of different materials are now being vigorously investigated in connection with the development of fuel cells employing different types of fuel. Thus the electrochemical system consists of the galvanic cell

$$^{-}\mathrm{CO} \mid \text{electrolyte} \mid \mathrm{O_2} + \qquad (1)$$

At constant pressure, the maximum amount of energy which may be obtained from an electrochemical current source is equal to the [decrease of the] free energy $-\Delta G$ of the reaction, described by the Gibbs–Helmholtz equation

$$-\Delta G = -\Delta H + T\Delta S = zFE\,, \qquad (2)$$

where ΔH is the change in the enthalpy of the system as a result of the reaction, T the absolute temperature, ΔS the change in the entropy of the system as a result of the reaction, z the number of electrons involved in the electrochemical reaction, E the e.m.f. of the current source, and F the Faraday.

Since the heat of reaction $Q = -\Delta H$, it follows that

$$zFE = Q + T\Delta S \qquad (3)$$

and further $E = Q/zF + T(\partial E/\partial T)_p$, where $(\partial E/\partial T)_p = \Delta S/zF$ is the temperature coefficient of the e.m.f.

According to Eqn.(3), the e.m.f. depends not only on the heat of the reaction in the current source, but also on the entropy term $T\Delta S = TzF(\partial E/\partial T)_p$. If $(\partial E/\partial T)_p > 0$ (the entropy increases so that $\Delta S > 0$), the e.m.f. increases with temperature.

The entropy change is equal to the difference between the entropies of the reaction products and the initial reactants:

$$\Delta S = \Sigma n_i S_{i_{prod}} - \Sigma n_i S_{i_{start}} \quad (4)$$

where n_i is the number of moles of the ith reactant.

The molar entropies of gaseous elements and many gaseous compounds differ little from one another and are considerably higher than the entropies of liquid and solid substances. In other words, since the degree of disorder in it is highest, the gas phase makes the greatest contribution to the entropies. Therefore $\Delta S > 0$ if the number of moles of the gaseous reaction products $n_{g.prod}$ is greater than the number of moles of the gaseous starting materials.

If $n_{g.prod} < n_{g.init}$, then $\Delta S < 0$, $(\partial E/\partial T)_p < 0$, and the e.m.f. decreases with temperature. If $n_{g.init} = n_{g.prod}$, then $\Delta S \simeq 0$, $(\partial E/\partial T)_p \simeq 0$, and the e.m.f. hardly depends on temperature, as, for example, the e.m.f. of the current source in which the following reactions take place:

$$CH_4 + 2O_2 \rightarrow CO_2 + 2H_2O,$$
$$C + O_2 \rightarrow CO_2.$$

For the reaction $2CO + O_2 \rightarrow 2CO_2$, $n_{g.prod} < n_{g.init}$ and therefore the e.m.f. of the current source in which carbon monoxide is oxidised electrochemically by oxygen decreases with temperature, as can be seen from Fig. 1 which includes for comparison the temperature dependence of the e.m.f. of the hydrogen–oxygen cell.

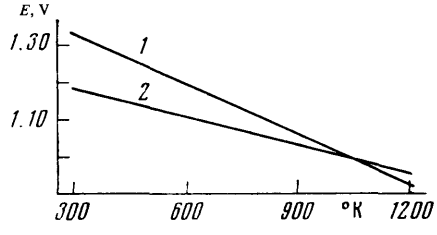


Figure 1. Temperature variation of the e.m.f.'s of gas cells: 1) carbon monoxide–oxygen cell; 2) hydrogen–oxygen cell.

The maximum (ideal) efficiency in the complete electrochemical oxidation of the fuel is

$$\eta = \frac{-\Delta G}{-\Delta H},$$

whence, using Eqns. (2) and (3), we obtain

$$\eta = 1 + T \cdot \frac{\Delta S}{Q}. \quad (5)$$

It is evident from Eqn. (5) that η may be greater than unity (i.e. greater than 100%) for a reaction with $\Delta S > 0$ ($n_{g.prod} > n_{g.init}$). In this case, the operation of the current source involves the removal of heat $\Delta Q = T\Delta S$ from the surrounding medium and its transformation into electrical energy. The cell itself does not become cold.

For example, a current source of this type would be one in which electrochemical oxidation of carbon occurs: $2C + O_2 \rightarrow 2CO$ (incomplete combustion of carbon).

In the electrochemical oxidation of carbon monoxide, $\Delta S < 0$, so that η of cell (1) decreases with temperature. This is evident from Table 1, which includes for comparison also data for the hydrogen–oxygen cell (Justi et al.[1], p. 32).

Thus the use of the carbon monoxide electrode in an electrochemical cell at a low temperature (not exceeding 100°C) under the conditions employed to develop active electrodes is more promising than at high temperatures, as was suggested at one time by Davtyan[2] and Daniel' Bek et al.[3] and comparatively recently by Chambers and Tantram[4].

Table 1.

Reaction	Z	T° K 300		600		900		1200		$\left(\frac{\partial E}{\partial T}\right)_p \cdot 10^3$
		E	η	E	η	E	η	E	η	
$2CO + O_2 \rightarrow 2CO_2$	4	1.33	0.91	1.2	0.81	1.06	0.72	0.92	0.63	0.445
$2H_2 + O_2 \rightarrow 2H_2O$	4	1.18	0.94	1.1	0.88	1.03	0.80	0.95	0.73	0.255

Justi and Grüneberg and coworkers, as well as other electrochemists including Soviet workers, have contributed to recent advances in the low-temperature electrochemical oxidation of carbon monoxide. One of the first attempts to employ the carbon monoxide electrode was in the Borchers cell (1894) (Davtyan[5], p. 39):

$$-CO\,(Cu)\,|\,HCl,\,CuCl\,|\,(Cu)\,O_2^+. \quad (6)$$

Borchers suggested that the electrodes were involved in the following reactions:

At the anode	At the cathode
$2Cl^- \rightarrow Cl_2 + 2e$,	$2Cu^{2+} + 2e \rightarrow 2Cu^+$,
$Cl_2 + CO_{soln.} + H_2O \rightarrow CO_2 + 2H^+ + 2Cl^-$	$^1/_2O_2 + 2Cu^+ + 2H^+ \rightarrow 2Cu^{2+} + H_2O$.
Overall process:	Overall process:
$CO_{soln.} + H_2O \rightarrow CO_2 + 2H^+ + 2e$.	$^1/_2O_2 + 2H^+ + 2e \rightarrow H_2O$.

However, the insignificant e.m.f. of this cell could not be due, according to some investigators, to the above reactions. Mond (Davtyan[5], p. 39) suggested that the e.m.f. of the Borchers cell is due to the electrodes employed. He justified this hypothesis by the fact that the replacement of the copper electrodes in the Borchers cell by carbon electrodes reduces the e.m.f. almost to zero. No data are available for the potential of the Borchers cell when the current is drawn to an external circuit.

More successful was the Hofmann cell[6,7]:

$$-\,CO\,(Cu)\,|\,KOH\,|\,(CuO,\,Cu)\,O_2\,+. \quad (7)$$

Here the potential close to that of the reversible hydrogen electrode is established at the copper|carbon monoxide electrode and Hofmann noted that this electrode gives a higher current for the same polarisation if the material of the electrode is partly in a carbon monoxide atmosphere (the idea which found a practical application in porous electrodes). The e.m.f. of this cell was 1.04 V, increasing to 1.17 V when platinum was employed as the material of the positive electrode. Apart from a fairly high e.m.f., another advantage of this cell when the electrode materials

described are employed is the use of an alkaline electrolyte in which copper is much more stable than in the electrolyte of the Borchers cell [cell (6)] and the rate of electrochemical reduction of oxygen is much higher. However, cell (7) suffers from the disadvantage that its electrolyte reacts with the product of the reaction.

3. KINETICS AND MECHANISM OF THE DIRECT ELECTROCHEMICAL OXIDATION OF CARBON MONOXIDE

Direct low-temperature electrochemical oxidation of carbon monoxide has been investigated at Group IB and VIII metals and also at tungsten, rhenium, and molybdenum. The electrodes were both smooth and porous (Raney type catalysts made of these metals were employed).

Table 2.

Electrode material	Soln. composition	Temp., °C	Steady-state potential on open circuit, mV: rel. to normal hydrogen electrode	Steady-state potential on open circuit, mV: rel. to hydrogen electrode in same soln.	Current density, mA per cm^{-2} of apparent surface	Polarisation, mV	References
Pt	0,1*N* H_2SO_4	25	—	+160	0.1	700	8
Pd	1,0*N* H_2SO_4	80	—	+85	—	—	9
Platinised Pt.	1*N* H_2SO_4	10—15	—	+170	—	—	10
Pt	ditto	30	—	00	—	—	10
Pt-DSC*	3*N* H_2SO_4	100	—	00	50	100	11
ditto	ditto	100	—	00	200	300	11
Pt	2*N* H_2SO_4	25	+360	—	—	—	12
Pt	1*N* $HClO_4$	25	—	—	4	800	18

*Double-skeleton catalyst electrode with a Raney platinum catalyst and a supporting framework made of gold powder (CO pressure 1.5 atm).

a. Acid Solutions

The experimental data available at present for the steady-state potentials of the carbon monoxide electrode made of different metals and their behaviour under the conditions of anodic polarisation are presented in Table 2 (the partial pressure of carbon monoxide is 1 atm throughout).

Almost all the few available data concerning sulphuric acid solutions demonstrate the difficulty of devising a carbon monoxide electrode in acid solutions. This is shown firstly by the finding that between 10° and 80°C the steady-state potential at platinum and palladium and platinised platinum electrodes not only does not approach the value for the reversible carbon monoxide electrode but does not even reach the potential of the reversible hydrogen electrode in this solution (Table 2). The only exception are data obtained recently by a group of German electrochemists for Pt-DSC † electrodes [11]. Secondly, this is indicated by the polarisation characteristics of the carbon monoxide electrodes made of these metals. At a smooth platinum electrode, an appreciable rate of electrochemical oxidation of carbon monoxide (about 0.1 mA cm^{-2}) is achieved only at a potential of 850–900 mV [8] and reaches a maximum (about 1 mA cm^{-2}) at a potential of 1000–1100 mV. The current depends both on the potential of the electrode (the state of its surface) and on the diffusion flux of carbon monoxide. On further increase of the potential, the current falls almost to zero owing to the passivation of the electrode by oxygen.

Recent data concerning the electrochemical oxidation of carbon monoxide in 3 *N* sulphuric acid are of considerable interest for the formation of a highly active carbon monoxide electrode at low temperatures [11]. The authors employed DSC electrodes about 1 mm thick comprising a Raney platinum catalyst. The steady-state potential of the carbon monoxide electrode measured at 100°C was 0.0 mV (Table 2), i.e. was more positive than the reversible carbon monoxide electrode only by 132 mV, while in experiments [1] in 5 *N* KOH (85°C) using Raney molybdenum as a catalyst, the steady-state potential was more positive than that of the reversible carbon monoxide electrode by 370 mV.

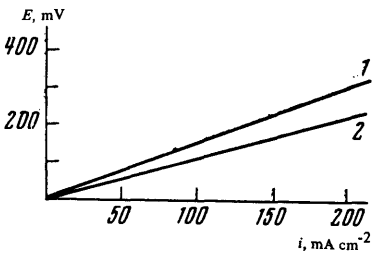


Figure 2. Steady-state polarisation characteristics of platinum DSC electrodes at 100°C (potentials given relative to the hydrogen electrode in the same solution): 1) carbon monoxide as depolariser; 2) hydrogen as depolariser.

Fig. 2 presents the steady-state polarisation characteristics for the electrochemical oxidation of carbon monoxide and hydrogen at a Pt–DSC electrode [11]. Evidently the rate of electrochemical oxidation of carbon monoxide at this electrode is fully comparable to the rate of electrochemical oxidation of hydrogen under these conditions for a not much higher polarisation. The polarisation characteristics of this Pt–DSC electrode in the electrochemical

† A double-skeleton catalyst electrode (Ed. of Translation).

oxidation of carbon monoxide are much better than in the electrochemical oxidation of hydrocarbons such as methane, ethane, and ethylene. Thus the kinetic parameters available at present for the carbon monoxide electrode in acid solutions are satisfactory.

The process mechanism has been considered by many investigators, who established that the carbon monoxide adsorbed on platinum and palladium exists in two forms (Young [13], p. 30; Fasman et al. [14]): a bridge form (8a) and a less stable linear form (8b).


(8a)


(8b)

Carbon monoxide is adsorbed when the *d* shell of the metal contains unfilled levels [15] and the greater the number of *d* vacancies the more stable the adsorption bond. The fraction of *d* vacancies in palladium is 0.55 per atom [16] and the metal can form fairly stable chemical compounds with carbon monoxide. Their stability depends on the pH: [9] in alkaline solutions, they are less stable and are located on the surface of the electrode, while in acid solutions they penetrate also the crystal lattice of the metal and decompose only at an elevated temperatures.

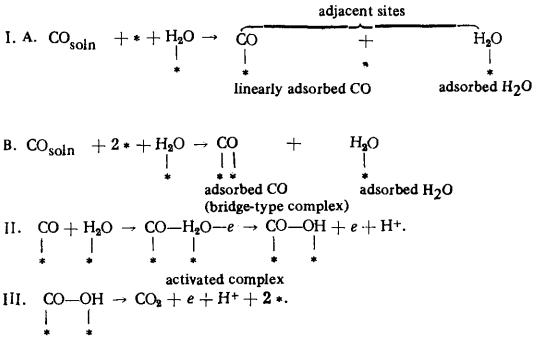
Accordingly, when carbon monoxide is introduced on platinum in 1 *N* sulphuric acid [10] at a potential of 500 mV relative to the hydrogen electrode in the same solution (the so called double layer region) at 50–70°C, the potential shifts to 50–70 mV in 30–60 min. Then it begins to move slowly towards positive values, because at 10–15°C carbon monoxide undergoes physical adsorption and at 20–30°C CO is converted into CO_2 and H_2 by the reaction

$$CO + H_2O \rightarrow CO_2 + H_2 . \qquad (9)$$

At 50–70°C the conversion of carbon monoxide is accompanied by its stable chemisorption (the formation of bridge-type bonds) and the hydrogen formed initially is displaced from the surface of the electrode. Thus at 50–70°C the potential–time curve has a minimum which can be accounted for by the onset of the conversion of carbon monoxide. This is confirmed also by the analysis of the gas phase when the electrode is saturated with carbon monoxide. The maximum carbon dioxide and hydrogen contents were observed precisely at 20–30°C. [10] Similar relations are observed in the adsorption of carbon monoxide on palladium [9,17].

The form of the potential–time curves [10] leads to the conclusion that, in contrast to 1 *N* H_2SO_4, in 1 *N* $HClO_4$ on platinised platinum there is no conversion of CO, since, after the attainment of a steady-state potential, the latter no longer changes in the temperature range 10–50°C. In this case surface compounds with weak and stable bonds are formed.

The mechanism of the step involving the electrochemical oxidation of carbon monoxide in 1 *N* $HClO_4$ at a platinum electrode was investigated by Gilman [18] in a stirred CO-saturated solution through which a triangular potential pulse was applied at a rate of 0.04 V s^{-1} at potentials between 400 and 1800 mV (relative to the hydrogen electrode in the same solution). Up to a potential of 700 mV, the current was very low, reaching a maximum of approximately 4 mA cm^{-2} at a potential of 800 mV. Subsequently the current fell sharply and then increased again only at 1550 mV, owing to the evolution of oxygen. When the potential was varied in the opposite direction, the curve had a different form. Gilman suggests a three-stage mechanism for the electrochemical oxidation of carbon monoxide at a platinum electrode in an acid solution (* — active adsorption centre):



According to Gilman stages I (A and B) are very fast whatever the surface coverage not exceeding the equilibrium value, and their rate is determined by that of the diffusion of carbon monoxide. Stage II, which proceeds via the activated complex, determines the rate of electrochemical oxidation of carbon monoxide, which involves weakly adsorbed carbon monoxide. Stage III is fast.

The electrochemical oxidation of carbon monoxide,

$$CO + H_2O \rightarrow CO_2 + 2H^+ + 2e , \qquad (10)$$

in 2 *N* H_2SO_4 on polished platinum [12] is regarded as chemical oxidation of carbon monoxide by oxygen evolved on the electrode and chemisorbed in the atomic form. The oxygen atoms react rapidly with chemisorbed CO to form CO_2, which is desorbed from the electrode. As a result, platinum is freed for the adsorption of fresh CO molecules and the process mechanism can be represented as follows:

$$\begin{cases} Pt + H_2O \rightarrow Pt{-}O + 2H^+ + 2e , \\ Pt{-}O + Pt{-}CO \rightarrow Pt_2{-}CO_2 , \\ Pt_2{-}CO_2 \rightarrow 2\,Pt + CO_2 . \end{cases} \qquad (11)$$

In the same study [12], it was observed that the electrode potential varies comparatively little when the surface coverage by monoxide falls to zero, as can be seen from the following data:

	CO partial pressure, atm			
	1.0	0.1	0.0037	0.00
CO oxidation potential, mV (relative to the normal hydrogen electrode).	1.25±0.13	1.18±0.11	1.03	1.00±0.11

These data confirm that there is no direct electrochemical oxidation of carbon monoxide, since the potential should change more markedly with decrease of the surface coverage by carbon monoxide. In both investigations [12,18], it was concluded that the carbon monoxide molecule is not involved in electron exchange with the electrode. The difference between them is as follows: Gilman [18] postulates that carbon monoxide is oxidised via an activated complex with water, while Warner and Schuldiner [12] believe that it proceeds via the dissociation and adsorption of oxygen, the adsorption of carbon monoxide, and the chemical reaction between the adsorbed carbon monoxide and atomic oxygen according to Eqn. (11) with subsequent desorption of carbon monoxide.

It is at present difficult to make a well-founded choice between these two mechanisms. Probably the mechanism should depend on the nature of the metal and its capacity to adsorb carbon monoxide and water. The inhomogeneity of the surface of the metal, which involves the possibility that the process may occur via different mechanisms on its different parts, is also important.

The attainment of the hydrogen electrode potential at DSC electrodes [11] led the authors to the hypothesis that carbon monoxide reacts with water to form carbon dioxide and molecular hydrogen. However, under these conditions there is also a possibility of direct electron exchange between carbon monoxide and the electrode metal, since Raney catalysts reduce sharply the activation energy for the reaction. Therefore it may prove unnecessary for the reaction to proceed via an activated complex to reduce the activation energy and also there may be no need for the interaction with the surface oxides on the electrode metal or for the shift of the electrode potential towards positive values up to 1 V and above (relative to the hydrogen electrode in the same solution). The observation of DSC electrode potentials more negative than the reversible hydrogen electrode potential would confirm this possibility.

An important characteristic of platinum and gold electrodes is that in acid solutions (1 *N* $HClO_4$) at potentials in the region of 1.25 V (relative to the hydrogen electrode in the same solution), the electrode surface is poisoned during the oxidation of carbon monoxide at a constant potential [19]. The poisoning is due to the products of the competing electrode reaction involving the oxidation of CO to $(CO)^+$. The (CO^+) cation is removed slowly by electrochemical oxidation and subsequent slow desorption.

The capacity of the starting material to form a non-poisoning rather than a poisoning product is characterised by the selectivity constant S, which, like the rate constant kS for the electrochemical removal of the poison, i.e. $(CO)^+$, depends on the electrode material. According to these parameters, platinum is a better electrode metal than gold. For platinum, $S = 0.9742$ and $kS = 6.61 \times 10^{-2}$ s^{-1} and for gold, $S = 0.9148$ and $kS = 2.3 \times 10^{-4}$. [19]

b. Alkaline Solutions

The experimental data obtained hitherto for the steady-state potentials of carbon monoxide electrodes made of different metals and their behaviour under the conditions of anodic polarisation are presented in Table 3 (the partial carbon monoxide pressure is 1 atm throughout).

The data in Table 3 show that in alkaline solutions it is easier to form a carbon monoxide electrode with satisfactory polarisation characteristics. As in acid solutions, best results were achieved with DSC electrodes.

For a smooth copper electrode in 5 *N* KOH, there is a linear relation between the CO oxidation current and potential when the latter is varied from −100 mV (relative to the hydrogen electrode in the same solution) to 400 mV. [20] Next, anodic dissolution of copper begins and the current rises sharply. The negligible adsorption of hydrogen by the copper electrode leads to virtual absence from the polarisation curve for this electrode of the section corresponding to the oxidation of hydrogen. Moreover, copper has an exceptional hydrogen overvoltage [series (16)] and the probability of the evolution of hydrogen is low even at a potential of −100 mV. However, at a potential of 400 mV, the current density reaches not more than 10 $\mu A\ m^{-2}$, which is very low for such a high polarisation. There are no data for the dependence of the potential and the current on the diffusion flux at a copper electrode.

The rate of electrochemical oxidation of carbon monoxide at a smooth palladium electrode in 5 *N* KOH is very much higher [20]. Up to a potential of 100–120 mV (relative to the hydrogen electrode in the same solution), H_2 is oxidised and then up to a potential of 380–400 mV the oxidation of carbon monoxide takes place. Above this potential, the process reaches the region of the limiting current, which is approximately 150 $\mu A\ cm^{-2}$. At a palladium electrode, the current depends markedly on the diffusion flux.

Among DSC electrodes comprising different Raney catalysts, the most satisfactory electrode is one with a molybdenum catalyst, giving a current of 30 mA cm^{-2} for a polarisation of 130 mV at 83°C, which is comparable with the polarisation characteristic of the Ni–DSC hydrogen electrode (Justi et al. [1], pp. 246, 277).

Table 3.

Electrode material	Soln. composition	Temp., °C	Steady-state potential on open circuit, mV: rel. to calomel electrode	rel. to normal hydrogen electrode	Current density, mA per cm^2 of apparent surface	Current density, mA per cm^2 of apparent surface	Polarisation, mV	References
Ni-DSC*	5*N*KOH	83	−1130	—	—	30	75	
Cu-DSC*	ditto	90	−1170	—	—	50	200	
W-DSC*	»	83	−1210	—	—	5	200	
Mo-DSC*	»	83	−1200	—	—	30	130	
Cu	»	25	—	—	−100	0.01	500	20
Pd	»	25	—	—	−150	0.15	300	20
Pd	»	25	—	—	−150	0 40 (limiting current without stirring)	550	20
Pd	40% K_2CO_3 (pH)	27	—	−570	—	—	—	13
Pt	ditto	27	—	−545	—	—	—	13
Rh	»	27	—	−540	—	—	—	13
Os	»	27	—	−520	—	—	—	13
Ir	»	27	—	−510	—	—	—	13
Ru	»	27	—	−475	—	—	—	13
Re	»	27	—	−469	—	—	—	13
W	»	27	—	−462	—	—	—	13
Cu	»	27	—	−190	—	—	—	13
Au	»	27	—	−150	—	—	—	13
Ni_3S_2	6 *N*KOH	25	—	—	−60			21
Ni_3S_2	ditto	75	—	—	−180	380	380	21

*Double-skeleton catalyst electrode comprising a Raney catalyst made from the given metal (Justi et al. [1], p. 246).

At a new electrode comprising the nickel sulphide (Ni_3S_2) catalyst in 6 *N* KOH, steady-state potentials of −180 and −60 mV at 75° and 25° respectively have been attained [21], these being the most negative values found for alkaline solutions (Table 3). However, they are far from the thermodynamic electrode potentials of the CO/CO_3^{2-} system. At a potential of 200 mV and a partial CO pressure of 1 atm in the same system at 75°C, the current reaches 80 mA per cm^2 of the apparent surface. In 1 M K_2CO_3 + 1 M $KHCO_3$ at 75°C and a potential of 180 mV, the current reaches 0.1 mA cm^{-2}. [21] It is extremely interesting that at the nickel sulphide electrode the oxidation of carbon monoxide is selective and H_2, NH_3, methanol, and formate ions present in solution are not oxidised. Therefore, bearing in mind that at a constant potential the CO electrochemical oxidation current is proportional under these conditions to the carbon monoxide concentration, such an electrode can be used as an indicator in the electrochemical determination of carbon monoxide.

Two mechanisms have been proposed for the electrochemical oxidation of carbon monoxide in alkaline solutions. One of these was proposed by Hofmann, who investigated cell (7), and Grüneberg (Justi et al.[1], p. 243), who studied the process at Cu–DSC and Ni–DSC electrodes in alkaline solutions. According to these investigators, the electrode process proceeds via a preliminary purely chemical stage with subsequent electrochemical oxidation of the hydrogen formed:

$$CO + 2OH^- \rightarrow CO_3^{2-} + 2H_{ads} \quad \text{(chemical stage)}, \qquad (12a)$$

$$2H_{ads} \rightleftarrows 2H^+ + 2e \quad \text{(electrochemical stage)}. \qquad (12b)$$

Grüneberg found that the following reactions can also take place at Ni–DSC electrodes:

$$CO + OH^- \rightarrow HCOO^- \quad \text{(chemical stage)}, \qquad (13a)$$

$$HCOO^- + OH^- \rightarrow CO_3^{2-} + 2H_{ads}$$

$$2H_{ads} \rightleftarrows 2H^+ + 2e \quad \text{(electrochemical stage)}. \qquad (13b)$$

Hofmann and Grüneberg justified these conclusions on the basis of the experimental finding that, when carbon monoxide is passed over Raney nickel and Raney copper electrodes, the latter attain the reversible hydrogen electrode potential to within 20 mV. However, Hofmann and Grüneberg's hypotheses cannot be regarded as convincing, since potentials significantly more negative than the reversible hydrogen electrode value have now been attained at the copper electrode in the same solution (Table 3). Grüneberg's postulate concerning the course of reactions (13a) and (13b) also cannot be regarded as final, since, firstly, the hydrogen electrode potential of the Ni–DSC electrode is established with a low reproducibility and, secondly, the hydrogen overvoltage of this electrode is insignificant. Therefore the slight shift of the potential towards negative values from the reversible hydrogen electrode value causes liberation of hydrogen, which resists this shift. Consequently another mechanism for the electrochemical oxidation of carbon monoxide, proposed by Justi et al.[1] (p. 244) and by Miller et al.[8], which accounts for the fact that the potential of certain metals is more negative than that of the reversible hydrogen electrode (this cannot be explained on the basis of the Hofmann–Grüneberg mechanism), is more likely:

$$CC_{ads} + 2OH^-_{ads} \rightarrow \underset{\downarrow K_2CO_3}{CO_2} + H_2O + 2e \quad . \qquad (14)$$

When the reversible hydrogen electrode potential is attained, the reduction of H^+ ions, the rate of which is determined by the electrode potential and the hydrogen overvoltage of the electrode material, becomes possible together with the oxidation of carbon monoxide. The hydrogen liberated consumes a certain number of electrons, which increases the rate of electrochemical oxidation of carbon monoxide without electrons being given up to the external circuit. This reduces the coefficient of utilisation of carbon monoxide when a carbon monoxide electrode is used in electrochemical cells. Thus, at potentials more negative than the hydrogen electrode potential in the same solution, two reactions [reactions (14) and (15)] take place simultaneously on the electrode:

$$2H^+ + 2e \rightarrow H_2 \rightleftarrows 2H_{ads} \quad . \qquad (15)$$

Reaction (15) is secondary. The hydrogen liberated as a result of this process is adsorbed on the electrode, reducing its capacity to adsorb carbon monoxide and possibly occupying active centres on the electrode surface.

The reversible carbon monoxide electrode potential can be approached only for electrodes with a significant hydrogen overvoltage. It is then necessary to bear in mind the following series of metals in terms of their hydrogen overvoltages (Frumkin et al.[22], p. 154):

$$\underset{\text{increase of hydrogen over voltage}}{\overset{\text{increase of catalytic activity in recombination of H atoms}}{\longleftarrow \text{Pt, Pd, W, Ni, Fe, Ag, Cu, Zu, Sn, Pb} \longrightarrow}} \quad . \qquad (16)$$

Therefore the carbon monoxide electrode potential obtained for palladium, which has a much higher hydrogen overvoltage than platinum (Antropov[23], p. 352), was appreciably more negative than the potential of the reversible hydrogen electrode (Table 3). However this is not easy to achieve and not all the investigators obtained such a potential for palladium[9].

A platinum electrode potential more negative than that of the reversible hydrogen electrode has not been obtained[13]. On the other hand, the steady-state carbon monoxide electrode potentials of copper and gold[24], which have a significant hydrogen overvoltages according to series (16), are closer to the reversible value (Table 3).

Analysis of the literature data shows that, as in acid solutions, a high electrochemical activity in relation to carbon monoxide in alkaline solutions requires that the electrode metal should have unfilled *d* orbitals. The electrode potential of the carbon monoxide electrode (and the free energy to which it is proportional) are approximately proportional to the heat of chemisorption. Therefore a stronger bond between carbon monoxide and the chemisorbing metal (a higher heat of chemisorption) increases the irreversible losses of free energy and decreases the steady-state electrode potential.

Evidently a potential close to that of the hydrogen electrode in the same solution is established for palladium (Table 3, Young[13]), while in more alkaline solutions a still more negative potential, up to −150 mV, is reached (Table 3, Tyurikova[20]).

4. ELECTROCHEMICAL OXIDATION OF CARBON MONOXIDE IN THE PRESENCE OF ELECTRON TRANSFER REAGENTS (VARIABLE-VALENCE IONS) AND OF HOMOGENEOUS CATALYSTS

In the electrochemical oxidation of carbon monoxide, the reaction product is carbon dioxide which is absorbed by the electrolyte in alkaline solutions, decreases the activity of the alkali, and impairs the operation of the carbon monoxide electrode. Therefore the use of acid solutions, where this difficulty is absent, would appear to be more promising. However, the materials for DSC electrodes employed in such solutions are very expensive[11]. The difficulty might be resolved on the basis of recent studies of the electrochemical oxidation of carbon monoxide in acid solutions with the aid of variable-valence ions, which are sometimes referred to as electron transfer reagents. Apart from the sharp increase of the rate of reaction at smooth electrodes, an advantage of this procedure is the possibility avoiding the use of a complex system such as porous electrodes.

The guiding factor in the choice of electron transfer reagents is that the potential of their oxidation-reduction transition should be more positive than that of the reversible hydrogen electrode in the given solution and the redox system should be readily regenerated by carbon monoxide.

The effect of complex salts of palladium(II), rhodium-(III), and platinum(IV) [25] and also of ruthenium(IV), osmium(IV), and iridium(IV) [26] on the kinetics of the reduction of $Cr_2O_7^{2-}$, IO_3^-, Fe^{3+}, $[Fe(CN)_6]^{3-}$, Cu^{2+}, and Sn^{4+} ions by carbon monoxide in the liquid phase has been investigated. The rate of reduction in the presence of the above homogeneous catalysts varies in parallel with the standard oxidation-reduction potentials of the corresponding redox systems. The values of these potentials (E_0) at 25°C are presented in Table 4 (Vetter [27], p. 61).

Table 4.

Redox system	Electrode reaction	E_0, mV (rel. to normal hydrogen electrode)
$Cr^{3+}/Cr_2O_7^{2-}$	$2Cr^{3+} + 7H_2O \rightarrow Cr_2O_7^{2-} + 14H^+ + 6e$	+1330
I_2/IO_3^-	$^1/_2I_2 + 3H_2O \rightarrow IO_3^- + 6H^+ + 5e$	+1195
Fe^{2+}/Fe^{3+}	$Fe^{2+} \rightarrow Fe^{3+} + e$	+771
$[Fe(CN)_6]^{4-}/[Fe(CN)_6]^{3-}$	$[Fe(CN)_6]^{4-} \rightarrow [Fe(CN)_6]^{3-} + e$	+360
Cu^+/Cu^{2+}	$Cu^+ \rightarrow Cu^{2+} + e$	+158
Sn^{2+}/Sn^{4+}	$Sn^{2+} \rightarrow Sn^{4+} + 2e$	+150

Thus the reducible ions investigated can be arranged in the following sequence:

$$\xrightarrow[\text{increase of standard redox potential and of rate of reduction by carbon monoxide}]{Sn^{4+},\ Cu^{2+},\ [Fe(CN)_6]^{3-},\ Fe^{3+},\ IO_3^-,\ Cr_2O_7^{2-}} \quad (17)$$

In terms of their activity, homogeneous catalysts can be arranged in the series $Pd^{2+} > Rh^{3+} > Pt^{4+}$ and the most active catalysts are the acido-complexes of the anion $[PdBr_4]^{2-}$. The rate of reduction by carbon monoxide is proportional to the amount of catalyst at its low concentrations and tends to a limit at high concentrations [25]. An excess of Cl^- ions inhibits the reduction reaction and an excess of Br^- ions accelerates it. In conformity with the laws of chemical kinetics, the experimental rate of reduction of the redox system is directly proportional to the partial pressure of carbon monoxide.

Carbon monoxide is readily adsorbed on copper and palladium. However, the dissolution of copper in acid solutions rules out its employment as the electrode metal. The first studies on the electrochemical oxidation of carbon monoxide at platinum and palladium using the Cu^+/Cu^{2+} redox system are now being made. The mechanism of the anodic process involving the Cu^+/Cu^{2+} system is described by the reaction

$$2CO + 2H_2O + 4Cu^{2+} \rightarrow 4Cu^+ + 2CO_2 + 4H^+ . \quad (18)$$

When this type of electrode is employed together with an oxygen electrode, the following overall reaction takes place at the cathode of the resulting cell:

$$O_2 + 2H_2O + 2e \rightarrow 2H_2O_2 + 2e \rightarrow 4OH^- . \quad (19)$$

The overall process in the carbon monoxide–oxygen electrochemical cell is

$$2CO + 4Cu^{2+} + O_2 \rightarrow 4Cu^+ + 2CO_2 . \quad (20)$$

The amounts of water consumed and formed in reaction (20) are identical. Thus water serves as an agent transferring oxygen from the cathode to the anode. The role of the redox system reduces to the transfer of electrons from the CO molecule to the anode. The redox system is regenerated by oxidation at the anode. The reaction product (carbon dioxide) is removed from the solution as it is formed.

However, the current densities obtained when the Cu^+/Cu^{2+} system is employed amount to several mA cm^{-2}. Such low current densities can be apparently accounted for by the fact that, although the redox system has a sufficiently negative E_0 (Table 4), according to series (17) the rate of reduction of the Cu^{2+} ion by carbon monoxide is low. Moreover, at this current density the electrode potential is markedly displaced towards positive values, which makes this redox system relatively unsuitable for use in electrochemical cells at the present stage of development. It is also necessary to investigate the effect of the Cu^+ and Cu^{2+} additives introduced into the electrolyte on the oxygen electrode.

5. THE PROBLEM OF THE ELECTROLYTE IN THE ELECTROCHEMICAL OXIDATION OF CARBON MONOXIDE

Until comparatively recently, the choice of an electrolyte for the electrochemical oxidation of carbon monoxide involved a vicious circle, which now can be regarded as having been broken. The point is that the rate of electrochemical oxidation of carbon monoxide in acid solutions at smooth electrodes is negligibly low (and porous electrodes have begun to be used only comparatively recently). In alkaline solutions, where not only the rate of electrochemical oxidation of carbon monoxide but also the rate of electrochemical reduction of oxygen is higher, the electrolyte absorbed the carbon dioxide formed, which entails a decrease in the activity of the alkali and impairment of the operation of the carbon monoxide electrode.

This difficulty was partly overcome for alkaline electrolytes by the suggestion of Matusevich and Bagotskii [28], who investigated the effect of carbon dioxide passed through a weakly alkaline electrolyte on the pH of the solution. In such a solution, carbonate and bicarbonate are in equilibrium:

$$CO_3^{2-} + CO_2 + H_2O \rightleftarrows 2HCO_3^- , \quad (21)$$

and the presence of OH^- ions is ensured by the hydrolysis of the bicarbonate. The alkalinity of the solution increases as the equilibrium in reaction (21) shifts to the left with increase of temperature. It was found that at 98°C this type of electrolyte, consisting of $K_2CO_3 + KHCO_3 + H_2O$, at an overall concentration between 3 and 5 N and with constant flow of carbon dioxide, undergoes hardly any change in pH. However, this investigation refers to weakly alkaline solutions (pH not exceeding 10), which are employed comparatively rarely.

It has been stated that Justi and Winsell [29] developed a more promising method involving electrodialysis, whereby the absorption of carbon dioxide by alkali may be prevented. In the operation of a carbon monoxide electrode in an electrochemical cell, not more than 10% of the electrical energy generated by the cell is consumed in the electrodialysis.

A Pd-DSC electrode, which can work in both alkaline and acid solutions [29], has also been developed. In addition there is a Pt-DSC electrode [11] the characteristics of which in acid solutions are not inferior to those of DSC electrodes in alkaline solutions (Table 2). However, in acid solutions both these electrodes have to be made of precious metals, while the DSC electrodes for alkaline solutions require comparatively cheap metals such as nickel, copper, tungsten, and molybdenum.

At present, when the problem of the prevention of the absorption of carbon dioxide by alkaline solutions is close to being solved, the use of alkaline solutions with appropriate DSC electrodes is more justified. However, the future development of DSC electrodes will probably lead to the creation of cheap effective porous electrodes for acid solutions too.

Thus the development of porous electrodes, which has yielded important improvements by accelerating the electrode process and the ways of solving the problem of the electrolyte which have become apparent bring us closer to the achievement of the electrochemical oxidation of carbon monoxide at current densities acceptable in practice.

6. THE APPLICATIONS OF THE CARBON MONOXIDE ELECTRODE

From the very beginning, the carbon monoxide electrode was studied with the aim of its employment in electrochemical cells. The cells proposed by Borchers [5], Hofmann [6,7], Davtyan [2], Daniel' Bek et al. [3], and Chambers and Tantram [4] were of this kind. This is because carbon monoxide is a cheap fuel, which forms part of the gaseous waste from many industrial processes. It can also be obtained by the subterranean gasification of coal.

There has been a particular growth of interest in carbon monoxide electrodes in connection with the problem of fuel cells. The satisfactory results obtained recently in the electrochemical oxidation of carbon monoxide at DSC electrodes in alkaline solutions (Table 3) show that under certain conditions the carbon monoxide electrode is promising as a negative electrode in fuel cells with a weakly alkaline electrolyte.

The studies on the carbon monoxide electrode designed for use in electrochemical cell have created a basis for the development of electrochemical methods for the analytical determination of carbon monoxide. However, their practical application involves many difficulties. One must bear in mind that, when the hydrogen electrode potential in a given solution is attained, the evolution of hydrogen becomes possible. The rate of this process is determined by the electrode potential and the hydrogen overvoltage of the electrode material. The evolution of hydrogen involves the consumption of a certain number of electrons, which increases the rate of electrochemical oxidation of carbon monoxide without transfer of electrons to the external circuit. This may distort the variation of the current or potential with carbon monoxide concentration. If the electrode potential shifts towards values more positive than the hydrogen electrode potential in the given solution, the accumulated adsorbed hydrogen gives rise to an additional anodic current, which also distorts the proportionality between the current and the carbon monoxide concentration. Therefore, for the analytical determination of carbon monoxide, it is particularly necessary to create an electrode at which only the electrochemical oxidation of carbon monoxide would occur. This can be achieved in two ways: by maintaining the electrode potential in the range of values more positive than the hydrogen electrode potential in the given solution or by using an electrode metal with a higher hydrogen overvoltage.

Ovenden [30], who developed an amperometric method for the analytical determination of carbon monoxide at a palladium electrode, followed the first procedure. Moreover, according to series (16), palladium has a higher hydrogen overvoltage than platinum. The experiments were performed at a vibrating steel microelectrode coated with palladium, platinum, rhodium, and iridium at carbon monoxide concentrations in the phase analysed (air) between zero and 100%. The maximum sensitivity (current) and maximum linearity of the variation of the current with carbon monoxide concentration were obtained at palladium, which is the most effective catalyst, among all the metals investigated by Ovenden [30], of the reaction between carbon monoxide and oxygen, in agreement with a number of other data [13,20,29]. The limiting diffusion current at palladium is attained when the potential is between 1.4 and 1.5 V relative to the hydrogen electrode in the same solution. The electrolyte consisted of 0.1 M sodium phosphate (pH 7) and 0.1 M sodium borate (pH 10) buffers and the diffusion coefficients of carbon monoxide in these solutions were found to be respectively 2×10^{-5} and 5×10^{-5} $cm^2\ s^{-1}$. In water, the diffusion coefficient of carbon monoxide is $(2.5 \pm 0.1) \times 10^{-5}$ $cm^2\ s^{-1}$. In the borate buffer [30], the limiting diffusion current was approximately twice as high as in the phosphate buffer, which is due to the difference between the diffusion coefficients of carbon monoxide in these solutions. In the region of the limiting diffusion current in the $CO-O_2$ mixture, the dependence of the current on the carbon monoxide concentration is almost linear at carbon monoxide concentrations between 0 and 100% and independent of electrode polarisation. This shows that in this case the limiting current is fully diffusion-dependent, which is very important for analytical purposes.

Roberts and Sawyer [32], who developed a polarographic method for the determination of carbon monoxide at a gold electrode, which has a high hydrogen overvoltage (Antropov [23], p.352), followed the second procedure. They used spherical and plate electrodes in 0.01 N KOH + 0.1 N K_2SO_4 solution. In the recording of the polarogram at a potential of approximately −500 mV (relative to the saturated calomel electrode), a distinct current peak, controlled by the diffusion of carbon monoxide, was observed. This peak current follows the equation

$$i_p = 3.01 \cdot 10^5 n [n_\alpha (1-\alpha)]^{1/2} A D^{1/2} c v^{1/2} \qquad (22)$$

where n is the number of electrons involved in the electrode reaction, n_α the number of electrons involved in the rate-determining stage of the electrode reaction, A the area of the electrode surface (cm^2), v the rate of increase of potential ($V\ s^{-1}$), c the concentration of carbon monoxide ($mole\ cm^{-3}$), and α the transport coefficient of the electrode process.

The current peak was directly proportional to the carbon monoxide concentration in the range between 0 and 100% in a carbon monoxide–molecular nitrogen mixture, the relation being linear over the entire concentration range investigated. The error of the method is not more than ±2%.

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VODGEO Research Institute,
Moscow

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Heterophase Radical Polymerisation

V.A.Popov and G.P.Gladyshev

The review deals with the characteristics of the heterophase polymerisation of various monomers, the effect of the transition from a homogeneous to a heterogeneous system, and certain physical factors on the rate of polymerisation, the molecular weight of polymers, and the composition of copolymers. A general account is given of published data for the morphological structure of the polymer phase formed. The views of various investigators on the mechanism of the heterophase polymerisation are discussed and the kinetic mechanisms and models of heterophase polymerisation are examined critically.

The bibliography includes 164 references.

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I. INTRODUCTION

One of the thoroughly investigated chemical reactions is radical polymerisation, a quantitative theory of which was developed as early as the 1940s and the 1950s. However, there are many processes in this field which deviate from the laws of ideal radical polymerisation and their rigorous kinetic analysis constitutes a difficult problem.

Such processes include radical heterophase polymerisation, characterised by the segregation of the polymer formed in a new phase with simultaneous occurrence of elementary chain propagation and termination stages in the solid phases, which are separated in space but can communicate via liquid or gaseous phases. The polymerisation of vinyl compounds such as acrylonitrile, acrylic and methacrylic acids, ethylene, and its halogeno-derivatives (vinyl chloride, vinylidene chloride, vinyl bromide, tetrafluoroethylene, chlorotrifluoroethylene, etc.) have all the properties characteristic of heterophase polymerisation. The appearance of a new phase is a characteristic of ω-polymerisation, the copolymerisation of certain monomers (for example styrene and maleic anhydride, methyl methacrylate, and methacrylic acid), and also the polymerisation of the usual monomers (styrene, methyl methacrylate, vinyl acetate, etc.) in media which do not dissolve the polymers.

A number of technically important polymers and copolymers have been obtained by heterophase polymerisation. Recently a method for the synthesis of poly(vinyl chloride) in bulk, with improved mechanical properties, high purity, and resistance to the atmosphere, has been developed and applied in industry[1-5]. However, the difficulty of temperature control at later stages of the reaction owing to the low thermal conductivity of the solid polymer phase hinders the application of this method to other monomers.

The study of heterophase radical polymerisation is of considerable theoretical as well as purely practical interest. Consequently many studies have been made of heterophase polymerisation, some of which have been described in a series of monographs and reviews[6-10]. However, since these reviews are concerned solely with the polymerisation of individual monomers and only give a general account of the results of earlier studies, we thought it desirable to give a systematic account of the extensive data which have now accumulated. Moreover, in recent years, certain definite advances have been achieved in the interpretation of the kinetic data and in studies on the morphology of the polymer phase, which have made possible considerable progress towards understanding of the mechanism of the heterophase polymerisation and have yielded qualitative and semiquantitative theories which give a generally satisfactory description of its characteristics.

This review also describes the results of certain earlier studies which were not considered in the above reviews, but which are of considerable interest in the light of modern ideas. Problems involving ω-polymerisation have been excluded from consideration, since they have been described fairly completely in a number of monographs[6,11].

II. KINETIC AND CERTAIN OTHER CHARACTERISTICS OF POLYMERISATION WITH FORMATION OF A NEW PHASE

1. Effect of Transition from a Homogeneous to a Heterogeneous System on the Rate and Degree of Polymerisation

Early studies[6,12,13] on the kinetics of the polymerisation of acrylonitrile and vinyl chloride in bulk already revealed their significant difference from the kinetics of the homogeneous polymerisation of the usual vinyl monomers: in the first case, the reaction takes place with self acceleration from the beginning, has higher average velocities, and gives higher molecular weights of the polymers formed. It has been shown that these anomalous properties are due to the formation of an insoluble polymer during the reaction. In the studies of recent years, the autocatalytic nature of the kinetic curves was noted for many monomers undergoing heterophase polymerisation in bulk or in precipitating media -vinylidene chloride[14], ethylene[15,16], tetrafluoroethylene[17,18], acrylic[19] and methacrylic acids[20], styrene[21], acrylamide[22], and others[23,24]. For example, Ryska et al.[25] observed the acceleration of the reaction from the instant of transition from a homogeneous to a heterogeneous polymerisation system comprising vinyl chloride in diethyl oxalate. The acceleration period depends on the physical and chemical properties of the medium and can continue up to conversions of 2—3% (as for acrylic and methacrylic acids) or much higher values (40% and above, as in the case of vinyl chloride).

Heterophase polymerisation is also distinguished by the formation of polymers with higher molecular weights. Fig. 1 shows the variation of the degree of polymerisation of vinyl chloride in tetrahydrofuran (THF) with the initial concentration of the monomer in solution[26]. At a monomer concentration in excess of 9 M, the polymer formed is segregated from the solution and its molecular weight increases sharply on further increase of the amount of monomer in THF. If the rate constant for chain transfer to the monomer is low, the degree of polymerisation usually increases with conversion[15,16,27-29].

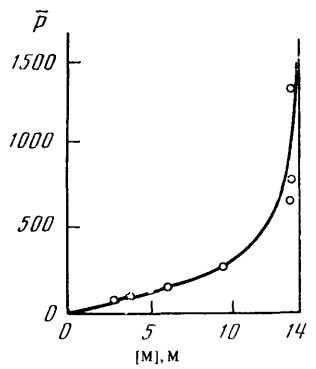


Figure 1. Variation of the degree of polymerisation of vinyl chloride with the initial monomer concentration [M] in THF.

The above anomalous phenomena in heterophase polymerisation (self acceleration, high average reaction rates and molecular weights of the polymers) are usually explained by a decrease of the rate of termination of the growing chains owing to the low mobility of the macroradicals in the solid phase. According to the theory of solutions of high-molecular-weight compounds[30], a macromolecule, in which there is an appreciable degree of freedom of rotation of the individual units relative to one another, coils up in solution. The structure of the coil depends on the solvent power of the medium. In "good" solvents, the coil has a very loose structure and is filled with solvent molecules to the extent of 95—99%.[9,31] In media which do not dissolve the polymer, the macromolecule and the macroradical becomes segregated from the solution in the form of a dense coil, access to the active radical of which is greatly hindered (the macroradical is occluded). Subsequent aggregation of the macromolecules into polymeric particles causes further blocking of the macroradicals and reduces the rate of chain termination—according to certain data[32], the rate constant for chain termination may decrease by 5—6 powers of ten. If one assumes that the rate of chain propagation does not change or changes insignificantly, because of the high mobility of the small monomer molecules, it becomes understandable why the rate of polymerisation increases following the appearance of the solid phase.

On decrease of the molecular weight of the polymer and after the introduction of active chain transfer agents, the self acceleration diminishes owing to the lower degree of occlusion of the macroradicals, the escape of small radicals (formed as a result of chain transfer) from the polymer particles to the liquid phase, and the increase of the rate of chain termination reaction[6,33,34].

One should recall that in certain studies[35] the above view on the nature of the self acceleration of heterophase polymerisation (occlusion of the active ends of macroradicals) is used also as a qualitative explanation of the "gel effect" in the polymerisation of certain vinyl monomers at advanced stages of the reaction.

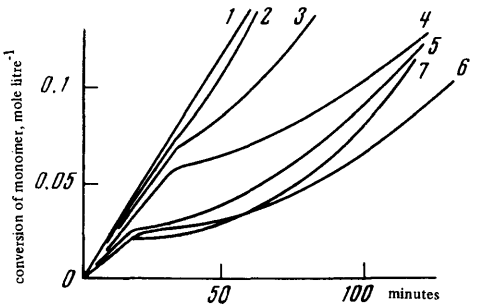


Figure 2. Polymerisation of vinyl chloride in diethyl oxalate at 25°C. The monomer concentration increases from 9.81 M (curve *1*) to 13.05 M (curve *6*). The breaks in the curves correspond to the formation of the polymer phase.

However, studies in recent years showed that, when the medium becomes heterogeneous, the morphological structure of the polymer phase, its swellability, the permeability of the polymer aggregates, the physical adsorption of monomer molecules on the solid phase, etc. have a marked influence on the rate of polymerisation. In many cases, at the instant when the medium becomes heterogeneous the polymerisation reaction is not accelerated but actually retarded, which indicates the influence of these physical factors not only on the chain termination reaction but also on the chain propagation reaction. Thus Ryska et al.[25], who studied the polymerisation of vinyl chloride in diethyl oxalate and 2,4-dichloropentane solutions, observed, on transition of the reaction from the homogeneous to the heterogeneous region, a stage with a sudden decrease of the rate followed by a rapid increase with conversion (Fig. 2). In the presence of an effective chain transfer agent (carbon tetrabromide), an increase of the ratio of the rates of chain transfer to carbon tetrabromide and of chain propagation was noted under heterogeneous conditions. On this basis, it was concluded[25] that transition to the heterogeneous region is accompanied by a decrease of the rate of chain propagation owing to the coiling up of insoluble macroradicals and their subsequent association, which hinders the access of the monomer molecules to the polymeric aggregates and reduces their local concentration in the vicinity of the active radical centres. According to approximate calculations of Bamford et al.[36], this local concentration of acrylonitrile is 1/180 of the macroconcentration of the monomer in the system. On the other hand, it is believed[25] that the rate of chain termination at the instant when the medium becomes heterogeneous changes less than might be

expected owing to the mutual approach of the active ends on association. However, as the amount of polymer increases, the rate of reaction rises with conversion, i.e. there is an acceleration effect owing to the further blocking of the macroradicals and a more marked effect of the solid phase on chain termination than on chain propagation.

Talamini and coworkers[37] observed a decrease of the initial rate of heterophase polymerisation of vinyl chloride in THF and in 1,2-dichloroethane with increase of monomer concentration. On the other hand, the average rate of reaction, measured at a specified degree of conversion, was always higher than in a homogeneous medium, owing to autocatalysis.

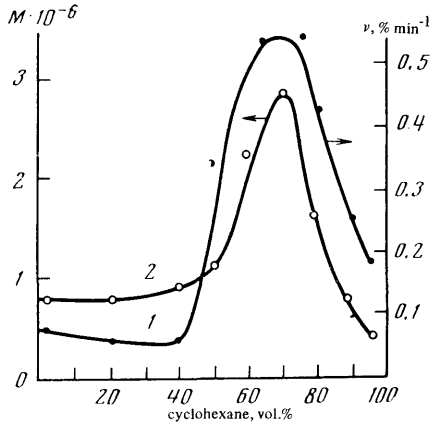


Figure 3. Variation of the maximum rate of polymerisation of methyl methacrylate (curve *1*) and the molecular weight of the polymer (curve *2*) with dilution of the monomer by cyclohexane at 55°C.

A decrease of the initial rate when the medium became heterogeneous was noted in the polymerisation of acrylonitrile in dimethylformamide (DMF) and ethylene carbonate[38] and of acrylic acid in methanol[39]. The variation of the maximum rate of polymerisation with the amount of precipitant in the methyl methacrylate system in cyclohexane was found to pass through a maximum[40,41] (Fig. 3). The authors explain these results by the influence of the swellability of the polymer phase, the permeability of the polymer aggregates, and the accessibility of the active centres on the elementary reactions. Since these factors depend on the type of polymer and solvent (or precipitant), the type of relation between the rate of polymerisation and monomer (or precipitant) concentration is different for specific monomers (vinyl chloride, acrylic acid, acrylonitrile, methyl methacrylate)[37-41]. When the precipitant content is high, the polymer phase is weakly swollen and the chain propagation reaction in it is retarded owing to the decrease of the local concentration of the monomer and its mobility in the relatively impermeable aggregate. The addition of solvent increases the swelling of the aggregate, which accelerates the diffusion of monomer molecules and increases the rate of polymerisation within the swollen particles. However, in the presence of a high content of the solvent, the increase of the mobility of the macroradicals and of the rate of termination of the growing chains plays a dominant role. Accordingly, the molecular weight of the polymers varies in parallel with the rate of polymerisation[37,38,40] (Fig. 3).

Somewhat different kinetic relation are observed in the polymerisation in a precipitant (cyclohexane) of acrylonitrile and acrylic and methacrylic acids, the polymers of which are incompatible with their monomers, in contrast to poly(methyl methacrylate)[41,42]. In this case, the rate of reaction decreases monotonically with dilution by cyclohexane, since access by monomer molecules to the occluded macroradicals is difficult owing to the incompatibility of the polymer and monomer and the low swellability of the polymer in the reaction medium. The unusual variation, involving a maximum in the dependence of the degree of polymerisation of acrylonitrile on temperature for the chemically initiated reaction, which was observed for the first time by Bamford and Jenkins[13] and Thomas and Pellon[12], is explained by the effect of swellability and mobility of the macrochains on the chain propagation and termination reactions:

Temperature, °C	30	40	50	60	70	80	90	100
Average molecular weight × 10^{-5}	4.3	6.25	8.64	10.73	6.36	3.76	2.17	1.38

Later similar results were obtained for the γ-initiated polymerisation of acrylonitrile[43] and ethylene[44].

An anomalous temperature effect was not noted[45] for vinyl chloride in the range 33–85°C owing to the high rate constant for chain transfer to the monomer. However, Talamini and Vidotto[46], who investigated its polymerisation at lower temperatures, found that the maximum molecular weight is reached at −30°C. According to another paper by the same investigators[47], the reason for this type of temperature variation is different degrees of crystallinity of the specimens obtained.

Bamford and Jenkins[48] examined certain cases of the secondary polymerisation of monomers initiated by macroradicals formed in the polymerisation of acrylonitrile (PAN) in bulk. The wide variety of kinetic curves obtained is due to the complex mutual relation between the swellability of PAN, the rate of diffusion of macroradicals and monomer molecules, and the kinetic characteristics of the process.

The rate of polymerisation of vinyl chloride in bulk at conversions less than 1% was found to be discontinuous by precise dilatometric measurements[49]. The study of the morphological structure of the solid phase formed made it possible to explain this decrease in the rate of polymerisation by the effect of the aggregation of macromolecules, which occurs on reaching the above conversions, on the elementary chain propagation and termination reactions.

Talamini and coworkers[37,38] examined the quantitative aspect of the decrease of the initial rate of polymerisation when the medium becomes heterogeneous. The reaction begins and continues in solution until the polymer concentration reaches a value such that the system separates into two phases. One of these is enriched and the other depleted in the polymer (we shall call these phases concentrated and liquid respectively). Using the steady-state hypothesis, the following expression was obtained for the ratio of the radical concentrations in the heterogeneous

and homogeneous systems before separation into different phases (Y):

$$Y = f_1^{1/2} \cdot v_1^{1/2} + \left(\frac{k_{tl}}{k_{tc}}\right)^{1/2} \cdot (1 - f_1)^{1/2} \cdot (1 - v_1)^{1/2} \quad (1)$$

where k_{tl} and k_{tc} are the rate constants for chain termination in the liquid and condensed phases respectively, v_1 is the volume fraction of the liquid phase, and f_1 the fraction of radicals formed per unit time in the liquid phase.

Eqn. (1) is valid also for the ratio of the rates of polymerisation in the heterogeneous and homogeneous systems on the assumption that the chain propagation rate constants remain unchanged. If $f_1 < v_1$ (the growing radicals and the polymeric molecules are more soluble in the concentrated phase) and $k_{tc} < k_{tl}$, the macroradicals pass to the concentrated phase at the instant of phase separation, y is less than unity, and the rate of polymerisation falls. The addition of a solvent accelerates polymerisation owing to the decreased probability of finding the growing chains in the precipitated phase. However, with increased conversion, Y becomes greater than unity faster the lower the value of k_{tc} compared with k_{tl}, i.e. phase separation gives rise to autocatalysis. For very high values of k_{tl}/k_{tc} (for example above 100), a decrease of the rate of polymerisation is observed only at low conversions (less than 1%). Autocatalysis becomes more pronounced with increasing conversion the more the growth of radicals in the concentrated phase predominates, i.e. the lower the solvent power of the medium.

An interesting effect of the presence of different phases on the conformation of polymethacrylic acid molecules was observed by Japanese workers[50]: in media precipitating polymers, the content of a syndiotactic polymer decreases owing to the active influence of the polymer phase on the addition of monomer molecules to the growing chain.

Thus the overall data presented above definitely demonstrate an active influence by the polymer formed not only on chain termination but also on chain propagation. It was shown that the apparent chain propagation rate constant decreases owing to the low swellability of the polymer (for example by 2—3 powers of ten in the polymerisation of acrylonitrile in bulk[32] compared with homogeneous conditions). Comparative analysis of the diffusion coefficients of low-molecular-weight substances in polymeric materials and of the rate constants for elementary reactions also demonstrates that, when the swellability of the polymer is low, the rate of chain propagation with $k_p > 10^2$—10^3 litre mole^{-1} s^{-1} is limited by diffusional parameters and not by kinetic parameters[51-55]. By altering the reaction medium and its interaction with the polymer, it is possible to influence actively the heterophase radical processes. For example, the rate of polymerisation of methyl methacrylate in methanol is much lower than in a methanol—water mixture owing to the greater swellability of the polymer and the higher mobility of macroradicals in the swollen solid phase in the first case[52].

The effect of pressure on the rate of heterophase polymerisation was studied by Gonikberg and coworkers[56-58], who observed an unusually marked acceleration of the polymerisation of butyraldehyde and isobutyraldehyde[56], α-methylacrolein[57], acrylonitrile[58], and methacrylic acid[20] at high pressures. This finding can be explained either by an increased rate of diffusion of the monomer in the polymer aggregates or by an increase of the degree of occlusion of the radicals (a decrease of the rate of chain termination).

When a chain transfer is introduced, the usual type of pressure variation of the rate and molecular weight is observed[58], which supports the second hypothesis. From this standpoint, one can understand the absence of anomalous phenomena in the polymerisation of vinyl chloride in bulk at high pressures[59,60].

2. The Role of the Polymer Phase in Heterophase Copolymerisation

The theory of homogeneous radical copolymerisation (in which the reactions are considered without considering the phase state of the system) makes it possible to calculate readily the composition of the copolymers when the relative activities of the monomers r_1 and r_2 are known. The study of the effect of heterogeneity on the composition of the copolymers led to the conclusion that the Mayo—Walling equation is inapplicable to heterophase copolymerisation. The majority of investigators[61-64] noted differences between the relative activities of the monomers of a particular binary system in different media. At present, the characteristics of heterophase copolymerisation can be accounted for solely on the basis of qualitative assumptions of different kinds.

Since the activity of comonomers is understood as the ratio of the chain propagation rate constants k_{11}/k_{12}, the deviations associated with the presence of the solid polymer can be explained by postulating that the rate of chain propagation reactions is determined by the rate of diffusion of the monomers to the active centres, or by a change in the elementary rate constants k_{11} and k_{12} owing to the specific features of the solid, or, finally, by the selective sorption of the monomers on the polymer phase, which leads to a change in the composition of the mixture of comonomers in the vicinity of the macroradical. Evidently the last factor has a major influence in the case of comonomers with markedly different polarities.

We shall consider certain experimental data using the sorption hypothesis. In this connection one must note the work of Brandrup[61,62] concerning the dependence of the composition of the copolymers of acrylonitrile and acrylic esters on the solvent. It has been shown that, on passing from a homogeneous to a heterogeneous system, the copolymer always becomes depleted in acrylonitrile as a result of a change in the water content in the solvent (DMF).

If the copolymerisation is carried out in water alone, then the copolymer is also always enriched in acrylic esters compared with homogeneous conditions. The lower the solubility of the acrylic ester in water the greater the probability of its incorporation in the copolymer. These findings can be readily explained if one assumes the preferential sorption of the less soluble acrylic esters by the polymer.

The above conclusion is confirmed also by the composition of the copolymers obtained in other precipitants (heptane, cyclohexane), where the opposite situation obtains, the copolymers being enriched in acrylonitrile relative to the initial mixture (Fig. 4). Since Brandrup's data show that acrylonitrile is less soluble in heptane and cyclohexane than acrylic esters, it is sorbed preferentially and its content in the copolymer increases.

Ryabov, Semchikov, and coworkers[40,42,65] found that, with increased concentration of the non-polar precipitant (cyclohexane) in the heterophase copolymerisation of methyl methacrylate with acrylonitrile, acrylic acid, or methacrylic acid, and also of vinylidene chloride with

acrylonitrile, the content of the more polar component in the copolymer increases. Since chain propagation occurs mainly within and on the surface of the polymer particles, i.e. in the zone of enhanced concentration of the sorbed polar monomer, this is responsible for its increased content in the copolymer. A definite piece of evidence supporting the selective sorption of one of the monomers is the decrease of the content of acrylic and methacrylic acids in the copolymers when the hydrogenated monomers (propionic and isobutyric acids) are added, which is due to the displacement of the unsaturated acids by the saturated acids from the sorption layers[66].

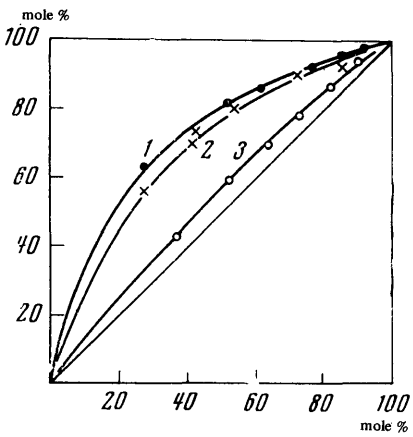


Figure 4. Composition curves for the acrylonitrile—ethyl acrylate copolymer in different media. The content of acrylonitrile in the copolymer is plotted against its content in the initial mixture: 1) heptane; 2) cyclohexane; 3) dimethylformamide (homogeneous media).

Graft copolymers of styrene with acrylonitrile or methyl methacrylate on polyethylene or Teflon are also enriched in the more polar monomer[67].

The local concentrations of the comonomers in the polymer phase $[M_i]_a$ may be related to their volume concentrations in the liquid phase $[M_i]$ by the Langmuir equation

$$[M_i]_a = \frac{k_{ad.\,i}[M_i]}{1 + k_{ad.\,i}[M_i]}; \quad i = 1.\,2 \qquad (2)$$

where $k_{ad.i}$ is the constant of the adsorption isotherm of the monomer in the polymer particles. Hence it follows that, when $k_{ad.1} \neq k_{ad.2}$, the composition of the copolymer formed in the solid phase $\{[M_1]_a/[M_2]_a\}$ will be different from the composition of the copolymer in the liquid phase $\{[M_1]/[M_2]\}$. The greater the difference between the constants k_{ad} the more pronounced is the inhomogeneity of the composition.

Moreover one should also expect a change in the rate constants for the elementary reactions. Thus copolymers with the same average composition (24% of potassium acrylate and 76% of acrylamide) obtained under homogeneous and heterogeneous conditions had different microstructures, i.e. different distributions of units in the chain, which indicates an effect of the solid phase on the elementary chain propagation reactions[64].

The curves describing the distribution of the compositions of the copolymers of acrylamide with maleic acid[68,69] and of methyl methacrylate with methacrylic acid[70] also form an anomalously broad peak compared with the theoretical curves, owing to the effect of phase heterogeneity on the chain propagation and macroradical recombination reactions.

Compared with sorption and the changes in rate constants, diffusion factors should have a smaller influence on the composition of the copolymers in view of the insignificant differences between the diffusion coefficients of the comonomers in such heterophase systems. For example, in the copolymerisation of acrylonitrile with methyl and propyl acrylates in bulk (heterophase conditions) and in the presence of an excess of acrylonitrile, the composition of the copolymers differs little from that obtained in the polymerisation in DMF solution. In this case, the rate of diffusion of monomers is so high that selective sorption is prevented[61].

If there is no preferential sorption of one of the monomers or if the added substance is a solvent for the copolymer causing its swelling and an increase of the rate of diffusion of the monomer molecules in the solid phase, phase heterogeneity has no effect whatever on the composition of the copolymer (provided that the chain-propagation rate constants remain unchanged); in this case the process has all the characteristics of homogeneous copolymerisation.

3. The Molecular Weight Distribution (MWD) of Polymers

Polymerisation involving the precipitation of the polymer formed is known to give rise to a broad or "irregular" molecular weight distribution with several maxima. Thus MWD of polyacrylonitrile obtained in dimethyl sulphoxide (homogeneous conditions) is much narrower than in the polymerisation of acrylonitrile in water (a heterogeneous system)[71]. A trimodal MWD was obtained by Pyrkov[72] in the polymerisation of acrylonitrile and by Eriksson[73] in the polymerisation of methyl methacrylate in water. Krozer and Czlonkowska[74] observed a distinct bimodal distribution for poly(vinyl chloride) polymerised in bulk at all conversions ranging from 18—78%. The MWD curves obtained by the fractional precipitation method for poly(vinyl chloride) polymerised in bulk also have two maxima[75]. Frenkel'[35] demonstrated for numerous instances of the polymerisation of acrylonitrile and vinyl acetate in water, vinyl acetate in heptane, ethylene under critical conditions, etc. that multimodal MWD is inevitably obtained in heterophase polymerisation. The multimodality arises as a result of the simultaneous occurrence of the elementary reactions in different phases (liquid and solid), each of which has its own characteristic monomer, radical, and initiator concentrations. In this case several distributions are superimposed. Part of the polymer is formed in solution and chain termination takes place in the liquid phase ($R^{\cdot} + R^{\cdot} \rightarrow P$); part of the growing macroradicals $P^{\cdot}$, trapped by the solid polymer particles, are deactivated either by the interaction of the dissolved macroradicals ($P^{\cdot} + R^{\cdot} \rightarrow P$) or by collision with another similar active polymer species ($P^{\cdot} + P^{\cdot} \rightarrow P$). This should result in a tri- or bimodal distribution function depending on whether chains are terminated by recombination or disproportionation. Fig. 5 presents trimodal

MWD for polyacrylonitrile obtained by polymerisation under heterogeneous conditions[35]. Evidently the distribution function is very broad and the ratio of the weight-average molecular weight of the polymer to the number-average molecular weight (P_w/P_n) is more than 10.

It has been shown[35] that detailed analysis of MWD and also of the variation of MWD with conversion may yield additional information about the mechanism of heterophase polymerisation, i.e. about the sites where chain propagation reactions occur, about the type of chain termination reaction, etc.

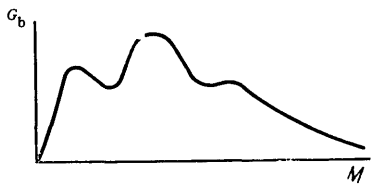


Figure 5. Molecular weight distribution of polyacrylonitrile obtained by the polymerisation of acrylonitrile in an aqueous medium; G_b—weight distribution function.

4. Post-polymerisation

The retardation of the rate of termination of macroradicals on formation of the solid phase leads to appreciable post-polymerisation. According to Magat's data[76], the rate of polymerisation of acrylonitrile in bulk decreased on switching off the radiation source to 1% of the initial value after 100 days and the conversion increased from 7 to 11%. The magnitude of the after effect depends on the duration of the initiated reaction[77].

Lyubetskii et al.[29] investigated the polymerisation of ethylene initiated by azobisisobutyronitrile at 70°C and a pressure of 100—600 atm. After cooling the system to 20°C ($v_{init} = 0$), the yield of polymer in 7 h increased from 125 to 156 g and the intrinsic viscosity increased from 1.10 to 1.70. Analogous results were obtained by Machi and coworkers[16,78,79].

Volkova and coworkers[17,18,80] observed an appreciable post-polymerisation of tetrafluoroethylene, vinyl fluoride, and vinylidene fluoride. Over a period of 60 min, the post-conversion of tetrafluoroethylene increased from 2 to 3.5% at 17.5°C. Fig. 6 illustrates the course of the post-polymerisation of acrylic acid in bulk at 20°C.[19]

Similar kinetic curves are characteristic of the post-polymerisation of acrylonitrile and vinyl chloride[32]. The after effect is appreciably suppressed with increase of temperature or when active chain transfer agents are introduced[32,43]. Analysis of the after effect can yield valuable information about the mechanism of the destruction of macroradicals, their lifetime, and kinetic constants.

If one assumes that in post-polymerisation macroradicals are destroyed as a result of bimolecular termination, it is easy to obtain the equations

$$\frac{1}{v_c} = \frac{k_t t}{k_p [M]} + \frac{1}{v_i}. \qquad (3)$$

and

$$\frac{\Delta [M]}{[M]} = \frac{k_p}{k_t} \ln ([R^\cdot] k_t t + 1), \qquad (3a)$$

where v_c and v_i are the rates of reaction at times t and $t = 0$ respectively. If chain termination proceeds via a mixed mechanism (bi- and mono-molecular)

$$-\frac{d[R]^\cdot}{dt} = k_t [R^\cdot]^2 + k_t' [R^\cdot], \qquad (4)$$

the following equation should hold:

$$\frac{\Delta [M]}{[M]} = \frac{k_p}{k_t} \ln \left(1 + \frac{k_p}{k_t'} [R^\cdot]\right) (1 - e^{-k_t' t}), \qquad (5)$$

where k_t' is the monomolecular chain termination rate constant.

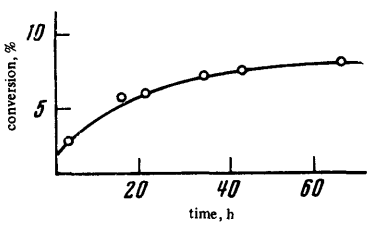


Figure 6. Post-polymerisation of acrylic acid at 20°C. The duration of polymerisation initiated by γ-irradiation was 20 min.

It has been found in a number of studies[32,43] that the post-polymerisation of acrylonitrile at 20—100°C and of vinyl chloride at −20°C is described by Eqns. (3) and (3a). However, in radiochemical polymerisation the linear relation $1/v_c = f(t)$ or $\Delta[M]/[M] = f(\ln t)$ has different proportionality coefficients at different conversions, which conflicts with the hypothesis that bimolecular chain termination with invariant k_t takes place. The authors attribute this to the occlusion of macroradicals. It has been shown that Eqn. (5) does not agree with the experimental data.

Markevich and coworkers[81] showed that Eqn. (3) holds for the dark polymerisation of tetrafluoroethylene in a precipitant (perfluorotriethylamine) and calculated k_t/k_p at 25°C. With increase of conversion, k_t/k_p decreases from 30 to 4 owing to the change in k_t. Under homogeneous conditions, the ratio k_t/k_p is constant at 70. k_p = 770 litre mole^{-1} s^{-1} has been determined by the method of inhibitors.

Using Eqn. (3a), Dainton and coworkers[82,83] found τ = 300 s for the polymerisation of acrylonitrile in water at 15°C, where $\tau = 1/k_t[R^\cdot]$. With increase of temperature to 30°C, τ falls to 150 s. The authors also concluded that the radicals in polymer particles are destroyed as a result of quadratic chain termination.

According to the data of Machi and coworkers[16,78,79], the rate of post-polymerisation of ethylene at a pressure of 250—400 atm increases with temperature in the range between 20° and 80°C, but remains constant for several hours at a specified temperature, which indicates the absence of chain termination reactions. However, at a

high temperature (140°C), the after effect is shown during a very brief period owing to the intense destruction of macroradicals.

Popov and Gladyshev[52] investigated the post-polymerisation of acrylonitrile in bulk at 17°C in the presence and absence of weak inhibitors of the type of diphenylamine (Fig. 7). It was shown that, when a solid phase is formed, the destruction of macroradicals takes place virtually at the instant of their interaction with the molecules of the weak inhibitor owing to the occlusion of active radical centres and the decrease of the rate of the R˙ + R˙ chain termination reaction; post-polymerisation is described by the equation

$$\ln \frac{v_{\text{нп}}}{v_c} = k_Z[Z](t - t_1) , \qquad (6)$$

where v_i and v_c are the rates of post-polymerisation at the initial instant t_1 and at any time t respectively, k_Z is the inhibition constant, and [Z] the concentration of the weak inhibitor.

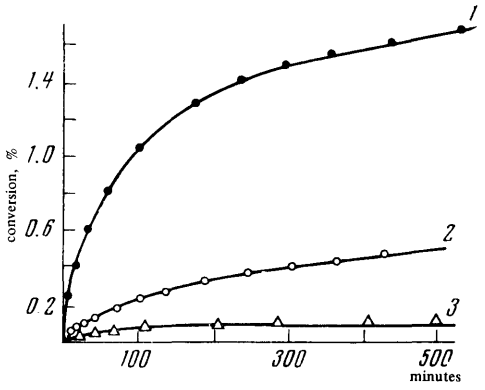


Figure 7. Post-polymerisation of acrylonitrile in bulk in the presence and absence of diphenylamine at 17°C; diphenylamine concentration (M): 1) 0; 2) 0.48×10^{-3}; 3) 1.21×10^{-2}. The polymerisation initiated by azobisisobutyronitrile (0.245×10^{-2} M) was continued up to a conversion of 3—3.5% at 60°C.

The constant k_Z was calculated from the linear relation between $\ln(v_i/v_c)$ and $t - t_1$ and was found to be 1.61×10^{-2} litre mole^{-1} s^{-1} for diphenylamine at 17°C. Thus the after effect method in heterophase polymerisation can yield valuable information about the reactivity of weak inhibitors of this kind, which previously could not be achieved in principle by the earlier Kise—Bagdasar'yan methods[11,84].

5. Quantitative Data

In heterophase polymerisation, the exponent n in the equation $v = k[M][I]^n$ is usually greater than 0.5. Thus, regardless of the method of initiation, $n = 0.8$ for acrylonitrile[7,85-87] and $n = 0.6$ for vinyl chloride[46,47]. An increased reaction order with respect to the initiator, which is characteristic also of other monomers undergoing heterophase polymerisation[6,16], is due to the occlusion of macroradicals and the catalytic effect of the polymer.

With increase of temperature, the degree of occlusion of active centres falls, the rate of termination rises, and n decreases to 0.5.[43,88]

The activation energy E_a for the polymerisation of acrylonitrile (thermochemical initiation) in bulk is fairly high, amounting to 35—37 kcal mole^{-1}.[12,89] With increase of temperature, E_a for radiation-induced polymerisation of acrylonitrile initially increases and then falls[43,90]:

Temperature, °C	0—20	20—60	60—70	70—90
E_a, kcal mole^{-1}	5	13.5—15	7.4	1.7

A similar relation between the apparent E_a and temperature was also found for methacrylic acid[88,91]: $E_a = 18.3$ kcal mole^{-1} at $T < 40°$, $E_a = 38.8$ kcal mole^{-1} at 40—75°C, and $E_a = 5.9$ kcal mole^{-1} at $T > 75$°C.

In the course of radiation-induced polymerisation of acrylonitrile, E_a increases up to a 20% conversion, then remains constant, and increases again at very advanced stages[92]:

Conversion, %	0	20—90	100
E_a (0-20°C), kcal mole^{-1}	4.65	6	10.4

The overall activation energy for the polymerisation reaction is defined as $E_a = E_p + nE_{init} - mE_t$, where $0.5 < n < 1.0$ and $m = 0.5$. Since E_t enters into this equation with a negative sign, the high value of E_a is evidently due to the diffusional component of the activation energy for chain propagation E_p and, in the case of thermochemical initiation, to the contribution of E_{init} owing to the increased value of n compared with homogeneous polymerisation. This equation also shows that E_t cannot be large. Indeed, according to certain experimental data, the chain termination activation energy for polyacrylonitrile[82,93,94] and poly(vinyl chloride)[95] under heterophase conditions is ~5—10 kcal mole^{-1} at $T < 100$°C.

The activation energy for the diffusion of macrochains in polymeric materials has been estimated as 25 ± 10 kcal mole^{-1}.[96,97] Since, as shown above, the active centres are deactivated by a bimolecular mechanism in heterophase polymerisation, the destruction of macroradicals is evidently not due solely to diffusion factors. Possibly, apart from quadratic chain termination, termination of the "relay" type as a result of chain transfer to the monomer and polymer, occurring by segmental and translational diffusion of macroradicals, plays an extremely significant role in this case.

This hypothesis is confirmed by a study of the heterophase polymerisation of certain monomers in the presence of weak inhibitors (inhibition constant $k_Z < 1$ litre mole^{-1} s^{-1}),[52] which are known not to affect the kinetics of homogeneous polymerisation. However, the sharp limitation of the rate of mutual termination of the growing chains when a solid phase is formed gives rise to a specific effect of relatively unreactive compounds of this kind owing to the increased importance of chain termination by the inhibitor. If the quadratic chain termination reaction may be neglected under certain conditions, it follows from the simplified mechanism that

$$v = \frac{k_p[M]}{k_Z[Z]} v_{in} , \qquad (7)$$

and

$$\bar{P} = \frac{k_p[M]}{k_Z[Z]} \qquad (8)$$

where [Z] is the concentration of the weak inhibitor. It has been shown that the rate of polymerisation of acrylonitrile in bulk decreases sharply from the very beginning

when small amounts of diphenylamine are added (Fig. 8). The reaction proceeds at a constant rate at least up to 50–60% conversion. In this case Eqns. (7) and (8) are valid and were used to calculate the ratio $k_Z/k_p = 0.151$ at 60°C.

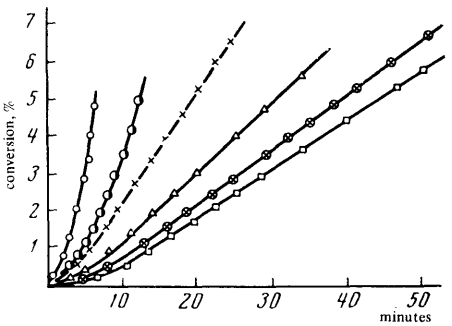


Figure 8. Polymerisation of acrylonitrile in bulk in the presence of diphenylamine at 60°C; concentration of azobisisobutyronitrile initiator 0.245×10^{-2} M; concentration of diphenylamine (M): 1) 0; 2) 0.12×10^{-2}; 3) 0.48×10^{-2}; 4) 1.21×10^{-2}; 5) 2.42×10^{-2}; 6) 3.64×10^{-2}.

In the polymerisation of methyl methacrylate in decane (a precipitant), diphenylamine has almost no effect on the reaction kinetics[52]. Evidently the degree of swelling of the polymer is in this case sufficiently high for chain termination by the recombination of macroradicals. However, the rate of polymerisation falls appreciably in methanol as a precipitant and even more so in a methanol–water mixture[52]. In the latter case, Eqns. (1) and (8) are also valid. The calculated k_Z are of the order of 10^{-1}–10^{-2} litre mole^{-1} s^{-1}. Thus the apparent reactivity of relatively inactive compounds increases sharply in heterophase polymerisation.

The constant for chain transfer to the monomer $C_M = k_{tr}/k_p$ is of the order of 10^{-5} for acrylonitrile[85,98]; $k_{tr} \simeq 10^{-2}$ litre mole^{-1} s^{-1} when $k_p \simeq 10^3$ litre mole^{-1} s^{-1}. Consequently, when one considers the mechanism of polymerisation with formation of a new phase, one must take into account reactions of this type. On the other hand, with increase of temperature the importance of physical factors (swellability of the polymer, diffusion of the monomer, occlusion of macroradicals) decreases, which leads to normal values of E_a.[88,90] If the polymer can undergo appreciable swelling, the overall activation energy is also close to the usual value, which has been noted, for example, for vinyl chloride (according to Gerren's data[99] the solubility of vinyl chloride in its polymer is 29% at 50°C and the constant for chain transfer to the monomer $C_m = 10^{-3}$).[26,100–102]

Some investigators[32,81,103] attempted to determine the rate constants for the elementary reactions. Thus Bawn et al.[32] found by the method of post-polymerisation that $k_p = 0.35$ and $k_t = 51$ litre mole^{-1} s^{-1} for acrylonitrile at 60°C and $k_p = 0.05$ and $k_t = 5$ litre mole^{-1} s^{-1} for vinyl chloride at −20°C. $k_p/k_t^{1/2}$ for acrylonitrile has a maximum at 50°C, which correlates satisfactorily with the temperature variation of the molecular weight[104]:

Temperature, °C	25	35	40	45	50	55
$k_p/k_t^{1/2}$	0.077	0.134	0.176	0.180	0.670	0.070

The values of k_p and k_t for ethylene calculated by different investigators show marked discrepancies[105–108].

Certain kinetic data may be obtained by studying heterophase polymerisation in the presence of inhibitors[52]. Then it is easy to calculate the ratio k_Z/k_p from Eqns. (7) and (8) and hence k_p if k_Z is known. On the other hand, k_p may be determined from the relation $v = k_p[M][R^\cdot]$ by measuring the concentration of macroradicals by the ESR method, since in the presence of an inhibitor the reaction proceeds under steady-state conditions. The values calculated for the polymerisation of acrylonitrile in bulk at 40°C are $k_p = 1.2$ and $k_t = 340$ litre mole^{-1} s^{-1}.

However, the observed rate constants for the elementary reactions are apparent values, since it was shown above that the rate of heterophase polymerisation depends on many factors and, moreover, there are not yet any quantitative data on the ratio of the monomer concentrations in the liquid and solid phases. However, first studies on these lines have been made[40,109,110].

III. MORPHOLOGY OF THE POLYMER PHASE

The first systematic studies on the morphology of the precipitated polymer were those of Thomas[10,12,111] on the polymerisation of acrylonitrile in bulk and in aqueous solution. At the beginning of the reaction (polymerisation in bulk), an opalescence appears with subsequent transition to a light turbidity. After 0.2–0.3% of the monomer has been converted into the polymer, the fine suspension of the polymer coagulates, forming a curd-like precipitate which fills the entire volume. When about 50% of the monomer has been converted, the reaction mixture consists of a white solid. Electron microscope studies showed that in the early stages the particles formed are dense globular, and identical in size. When the monomer conversion is about 1%, the particle diameter reaches 1000–2500 Å. The number of particles remains almost constant during the polymerisation process, and amounts to 10^{12}–10^{14} per cm^3 depending on the reaction conditions.

At high conversions (70–80%), a monolithic transparent solid is formed[112]. Kinetic studies on the polymerisation of acrylonitrile[89,112,113] and vinyl chloride[114] in bulk up to high conversions showed that the formation of a transparent polymer requires a correspondence between the rate of reaction and the rate of diffusion of the monomer molecules into the pores of the polymer particles. Under these conditions, the growth of the particles leads to close contact between them and to the disappearance of interfaces.

A series of studies dealing with the morphology of poly(vinyl chloride) polymerised in bulk and allowing a considerable understanding of the mechanism of the formation of the polymer phase were published in recent years[49,114–119]. In the initial stages of the process, the macromolecules are in a molecularly dispersed state in the monomer medium. When the degree of polymerisation of vinyl chloride exceeds 25–32, the macromolecules are no longer soluble in the monomer[49]. After the attainment of the critical concentration, the particles of a new polymer phase (possibly a polymer-monomer phase) are segregated. Their dimensions are determined by the

critical dimensions for nucleus formation. Bort[116] called these growing nuclei microglobules. Microglobules can grow both owing to the formation of the polymer within the particles and as a result of the adsorption of the polymer formed in the bulk of the monomer.

Microglobules are unstable with respect to aggregation and coalesce into macroglobules. According to the data of Cotman et al.[49], this occurs at a conversion of 0.2—0.9%. The morphology and number of macroglobules are influenced by the average rate of polymerisation, an increase of which entails an increase in the number of particles up to a constant value of about 10^{12} per cm^3.

In the course of polymerisation, new particles are not formed and their number remains constant. The number of microglobules in the macroglobule varies from 1 to several tens, depending on the rate of polymerisation. With increase of the degree of conversion, the size of the macroglobules increases from 0.1 to 1—2 μm. The narrow unimodal distribution of the particles with respect to size is evidence that the rate of growth remains almost constant for all the particles.

Since the globular structure persists up to 30% conversion and the number of particles remains unchanged during polymerisation, Bort et al.[116] reached the unambiguous conclusion that the increase in the mass of the globules is due to the macromolecules growing within the globules themselves rather than to those formed in the bulk of the monomer. Since the termination of the growing chains in the globule is greatly hindered, the rate of polymerisation in the particle will be higher than in the bulk of the monomer.

In the polymerisation of methacrylic acid in bulk, the polymer is also formed from the early stages as globules whose size is about 0.1 μm, which are then aggregated into larger globules[120]. In the general case, one assumes that the formation of the solid phase is closely related to the topochemistry of the polymerisation process, which in turn is determined by the nature of the interaction between the polymer and its monomer[118,121]. If the solvent power of the medium is sufficiently high for the formation of a monomer-polymer phase, i.e. a solution of the polymer in the monomer, the accumulation of the solid monomer may occur partly owing to the adsorption of the macromolecules from the solution on the surface of the polymer particles. Then the surface of the growing particle becomes "grown over". Consequently the structure of the particles may be varied from very dense to loose by a suitable choice of solvent[10,122]. In the presence of a large amount of solvent, the particles cease to be globular and the polymer consists of a monolithic mass, as shown for the polymerisation of methyl methacrylate in cyclohexane[40].

If the polymer particles produced are incapable of swelling, then the appearance of comparatively dense and smooth globular structures, owing to the settling on the surface of a fine "fraction" of the polymer from the liquid phase, is also to be expected.

The solid phase is formed somewhat differently in the polymerisation of monomers capable of crystallising. For example, in the polymerisation of vinylidene chloride, a mixture of lamellar crystals and globules is formed[14]. The presence of two types of structures in the reaction medium is due to the simultaneous occurrence of two processes: polymerisation and crystallisation.

Thus the characteristics of the morphological structure of the polymer phase formed depend on the polymerisation kinetics (the average rate of polymerisation), the swelling of the polymer particles, and the capacity of macromolecules to form part of crystalline structures.

IV. THEORIES AND KINETIC MECHANISMS OF HETEROPHASE POLYMERISATION

Analysis of the existing models of heterophase polymerisation reveals two opposed views concerning the site of the reaction in the formation of the polymer phase. According to the immobilised surface theory[45], the increase of the rate of polymerisation with conversion is explained by the increase of the area of the polymer phase formed. According to the occlusion theory[6], the mass of the polymer determines the characteristics of the heterophase polymerisation. There exist also other theories—in particular the heterophase polymerisation of certain monomers in water is regarded as analogous to polymerisation in emulsion[111].

The majority of the kinetic mechanisms are bases on the invariance of the rate constants for the elementary reactions, which constitutes an appreciable simplification.

1. The Surface Theory

The kinetic mechanism of Bengough and Norrish[45] is based on the fact that the polymer exhibits a cocatalytic activity on the polymerisation of vinyl chloride. The ease of chain transfer to the polymer leads to the formation of immobilised radicals and polymer particles. These radicals are almost incapable of bimolecular chain termination but do retain their capacity for growth. Growth continues until small mobile radicals are formed as a result of chain transfer via the monomer. In consequence of these transfer reactions, the chain returns to the liquid phase where bimolecular termination ultimately takes place.

The equation derived by the authors,

$$v = k[\mathrm{I}]^{1/2}[\mathrm{M}]\left\{1 + \frac{k'[\mathrm{P}]^{2/3}}{[\mathrm{M}]}\right\} \qquad (9)$$

where k and k' are constants and $[\mathrm{P}]$ is the amount of polymer per unit volume, shows that the rate of polymerisation is proportional to the amount of polymer raised to a power of 2/3, i.e. to the surface area of the polymer phase. According to this theory, the number of branches arising by chain transfer to the polymer is also proportional to conversion raised to a power of 2/3.[123]

Bearing in mind Bamford's critical comments[6] concerning the variability of the kinetic constants, Mazurek[124] derived the equation

$$v = v_i\,(1 + b[\mathrm{P}]^{2/3}), \qquad (9a)$$

where v_i is the initial rate of polymerisation and b the phase heterogeneity constant defined as the ratio of the rates of propagation in the polymer particles and in the liquid phase at a conversion of 1%. The following additional reactions were included in the usual kinetic mechanism:

$$\text{Transfer of radicals to the solid phase } R^{\cdot} \xrightarrow{k_a[\mathrm{P}]^{2/3}} R_a^{\cdot}$$

$$\text{Chain propagation in the solid phase } R_a^{\cdot} + M \xrightarrow{k_{pa}} R_a^{\cdot}$$

$$\text{Chain transfer to the monomer } R_a^{\cdot} + M \xrightarrow{k_{tra}} P + R^{\cdot}$$

where k_a is the rate constant for the transfer of radicals to the polymer phase and R_a are the radicals in the polymer phase.

It is assumed that the constant k_{pa} and k_{tra} vary with conversion but their ratio remains constant: $k_{pa}/k_{tra} \simeq$ const. On the basis of this mechanism, taking into

account the chain termination by radicals from different phases, and the concept of "live" polymer chains in the solid phase, Lyuberetskii and Mazurek[125] obtained an equation for the polymerisation of ethylene, which agrees satisfactorily with experimental data.

A mechanism has been proposed[86] for the polymerisation of acrylonitrile in water, which involves the adsorption and termination of macroradicals on the surface of polymer particles.

Certain indirect data also support the hypothesis that polymerisation takes place on the surface of the particles. Thus an interesting feature of heterophase polymerisation is the dependence of process kinetics on the physical state of the polymer formed, in particular on the particle size and hydrodynamic conditions[126-130]. For example, the rate of polymerisation of acrylonitrile, methyl acrylate, and methyl methacrylate falls on passing from a stable fine sol to a coarse polymeric precipitate, which may be attributed to the decreased surface area of the particles and the decreased number of radicals on the surface[127]. A similar effect was observed following the addition of electrolytes as coagulants[127,128]. On the other hand, the introduction of peptising agents or stabilisers into the system[82,127] (for example cetyltrimethylammonium bromide) increases the stability of the colloidal system and the rate of polymerisation. According to Chapiro[39], the kinetics of the polymerisation of acrylic acid in methanol are also determined by the form of the polymeric precipitate (gel or powder).

Roskin and coworkers[129,130] and Machi and coworkers[131] investigated the effect of stirring on the polymerisation of acrylonitrile in water and of ethylene in the gas phase. Electron photomicrographs led to the conclusion that the polymer-monomer particles approach one another on stirring, which increases the rate of collision of the globules and the rate of termination of the chains on their surface, decreasing the rate of polymerisation of acrylonitrile. Moor and Parts[132] found that the rate of polymerisation of acrylonitrile in the centrifuged polymeric precipitate is lower than in the suspension before separation. This may be due to the increased rate of chain termination when the particles are deposited, owing to their mutual approach and greater isolation of macroradicals from monomer molecules.

Dauphin et al.[44] believe that the role of the polymer phase reduces to an increase of the local concentration of the monomer owing to its adsorption on the polymer surface. However, it has been shown[133] that physical adsorption does not play the main role in the self-acceleration process. The above facts concerning the influence of the transition of the system to a heterogeneous state on the rate of polymerisation also constitute convincing evidence against this hypothesis.

2. The Occlusion Theory. The "Trapping" of Radicals

The immobilised surface theory of Bengough and Morrish[45], which is based on the ease of chain transfer reactions, is inapplicable to monomers such as acrylonitrile and tetrafluoroethylene and is not of general validity. Moreover, Eqn. (9) does not hold in the initial stages of the polymerisation of vinyl chloride (up to a conversion of about 8%).

Bamford and Jenkins gave a qualitative explanation of the characteristics of heterophase polymerisation on the basis of the occlusion theory†. Under conditions promoting the precipitation of the polymer, a macroradical, having reached a certain size, coils up to form a dense structure and is segregated from the liquid phase. The active end of the radical is then occluded in the coiled structure and the rate of the termination reaction falls significantly. During polymerisation, the macrochains coalesce into polymeric aggregates. The aggregation promotes further blocking of the radicals. It is postulated that aggregation entails an insignificant change in the rate of propagation compared with the rate of chain termination, which leads to an increase in the rate of polymerisation with time.

It follows from the occlusion theory that the self acceleration is not determined by the surface but by the mass of the polymer. According to this theory, polymerisation takes place within polymer particles, the degree of occlusion of the radicals and the magnitude of the polymer barrier preventing the penetration of the monomer to the radical end depending on the number and weight of the particles.

The occlusion theory is confirmed by many experimental facts. Thus one of its consequences is that the segregation of the monomer leads to anomalously long lifetimes and high concentrations of macroradicals. Indeed the overall concentration of macroradicals, determined by the ESR method, is 10^{-4}—10^{-5} M for various monomers[6,134-136]. For comparison, we may point out that in polymerisation in solution the concentration is less than 10^{-8} M (except at high conversions). The existence of long-lived radicals in the heterophase polymerisation of ethylene has been postulated by a number of workers[29,137].

If the initiating agent is removed in the initial stages of the polymerisation of acrylonitrile and the unreacted monomer is replaced by a fresh monomer, post-polymerisation is observed[6]. This shows that the radicals persist in the solid monomer and initiate the polymerisation of the fresh monomer. The concentration of these "trapped" radicals, determined by the ESR and inhibitor methods, is 10—13% of the total value, amounting to 7.8×10^{-5} M or 3.7×10^{16} spin ml^{-1} (at 20°C) [36] in a typical experiment.

With increase of temperature, the concentration of "trapped" radicals decreases appreciably[36]:

Temperature, °C	20	25	40	60
Number of "trapped" radicals per ml × 10^{-16}	3.7	2.3	0.8	0.1

Analogous results were obtained by Ingram et al.[134]

"Trapped" radicals have been detected by the ESR method in the polymerisation of methyl methacrylate and methacrylonitrile in hexane[135], in the polymerisation of methacrylic acid in bulk $\{[R^{\cdot}] \simeq 10^{-5}$ M$\}$,[138] in the polymerisation of other monomers[135,141], and in the copolymerisation of methyl methacrylate and methacrylic acid in benzene $\{[R^{\cdot}] = 10^{-4}$—10^{-5} M$\}$.[139] Kargin, Ryabov, and coworkers[120] found that the relation between the concentration of "trapped" radicals and conversion in the polymerisation of methacrylic acid in bulk passes through a maximum.

The "trapped" radicals can initiate the polymerisation of various monomers. Copolymers of acrylonitrile with vinyl acetate, vinylidene chloride, methyl methacrylate, and styrene have been obtained in bulk in this way[140]. At low temperatures, when chain transfer to the monomer is

† This theory is discussed in detail in the monograph of Bamford et al.[6]

insignificant, "trapped" radicals were detected in poly(vinyl chloride); following the addition of DMF, they are activated and initiate the polymerisation of styrene and methyl methacrylate[142]. Bamford and Jenkins[48] investigated the kinetics of the polymerisation of various monomers initiated by "trapped" polyacrylonitrile radicals.

The occlusion theory is qualitative, since it is difficult to express the quantitative relation between the rate constants and the degree of occlusion.

An interesting quantitative interpretation of the kinetics of heterophase polymerisation has been made by Mickley et al.[26], who attempted to eliminate the contradiction between the occlusion and surface theories. The authors suggested that in the initial stages the rate of polymerisation is proportional to the amount of polymer formed, since polymer particles are fairly small and do not prevent contact between the radicals "trapped" within the particles and the liquid phase. After subsequent growth and aggregation of the particles, only a thin surface layer of the aggregates remains in contact with the liquid phase and radicals are "trapped" either owing to chain transfer to the surface of the particles or owing to the penetration of the macroradicals diffusing from the liquid phase to the active surface region of the particles. In this stage, the rate of polymerisation is proportional to the volume of this active layer or approximately to the area of the polymer phase, i.e. $[P]^{2/3}$. The following kinetic equation for the stage in which the rate of polymerisation depends on the polymer volume V_P was derived on the basis of the above mechanism:

$$v = k[M][I]^{1/2} + k[I]^{1/2}\frac{k_{trP}D_L[R_a]V_P}{D_L k_{tr}a} \qquad (10)$$

For the stage where the rate of polymerisation depends on the surface area of the polymer phase S_P, we have

$$v = k[M][I]^{1/2} + k[I]^{1/2}\frac{k_{trP}D_L'[R_a^{\cdot}]\delta S_P}{D_L k_{tr}a}, \qquad (11)$$

where $k = k_p k_{in}^{1/2}/k_t^{1/2}$, [I] is the concentration of the initiator, k_{tr} and k_{trP} are the constants for chain transfer to the monomer and polymer respectively, D_L' and D_L are diffusion coefficients in the liquid phase of the macroradicals and monomeric radicals respectively, $[R_a^{\cdot}]$ is the average concentration of radicals in the active volume, V_P and S_P are the total volume and total surface area of the polymer particles per unit volume of the system, δ is the depth of penetration of the radicals into the particle, and a is the ratio of the concentrations of the monomeric radicals on the surface and in the active volume of the particles.

The proportionality of the rate of polymerisation of vinyl chloride to [P] in the first stage and to $[P]^{2/3}$ in the second stage has been confirmed experimentally[26]. However the usefulness of the above equations is doubtful in view of the difficulty of evaluating some of the parameters.

Cotman et al.[49] made a critical examination of the equation of Bengough and Norrish[45] and suggested that instead of the power exponent 2/3 one should use in Eqn. (9) a variable exponent α depending on the polymerisation conditions. The variation of α with the rate of polymerisation indicates a more complex relation between v and [P] than suggested by Bengough and Norrish. The studies by Bort[114-118] on the morphology of the polymer phase formed made a definite contribution to the elucidation of the question of the site where the chain propagation reaction occurs. Bort[148] obtained experimental evidence showing that the polymerisation of vinyl chloride takes place within the polymer particles, since a change in their surface area for a fixed mass of the polymer does not affect the form of the kinetic curves (except at high rates of polymerisation). Consequently the increase in surface area during heterophase polymerisation is not a factor responsible for self acceleration.

At high average rates of polymerisation, α approaches 2/3, which reflects the limiting relation between the rate v and the amount of polymer precipitated. In this case, the rate of polymerisation exceeds so much the rate of diffusion of macroradicals in the solid phase that there is not sufficient time during the chain propagation step for them to penetrate into the polymeric aggregate and therefore they remain on the surface. Moreover, the permeability of the aggregate decreases owing to the greater density of its structure at high rates of polymerisation and the increase of the polymer barrier to the diffusion of macrochains.

3. The Two-phase Model

Analysis of the morphological structure of the solid phase formed and of the kinetic data lead to the conclusion that in the general case the topochemistry of the polymerisation process is determined by the nature of the interaction of the polymer with the medium. It is possible to distinguish three regions where polymerisation takes place—the liquid phase, the surface, and the bulk of the polymer phase.

If the solvent power of the medium is sufficiently high for a solution of the polymer to exist, the polymer may accumulate largely owing to the formation of macromolecules in the solution. The usual kinetics of homogeneous polymerisation are characteristic of this process. When the swellability of the polymer is very low, the reaction takes place mainly on the surface and in the bulk of the particles formed. Kinetically, the radicals on the surface and in the bulk of the particles are non-equivalent, the activity of the latter being lower in the mutual termination and possibly propagation reactions.

On the basis of these concepts, Talamini[144] proposed a simple mechanism to describe the polymerisation of vinyl chloride in bulk. Since vinyl chloride is a poor solvent for its polymer (the Flory—Huggins constant for this system is 0.88 at 50°C [145]), the separation of the initially homogeneous system into two phases (a dilute liquid monomer-polymer phase and a concentrated solid polymer-monomer phase) takes place at very low conversions (about 0.1%). Subsequently the polymerisation process occurs simultaneously in both phases but at different rates, since the properties of the phases are different (viscosity, monomer concentration, etc.). With increase of conversion, the amount of the dilute phase diminishes and that of the concentrated phase rises. Assuming that the ratio of the rates of polymerisation in the two phases is constant, and that the kinetic constants do not vary with conversion, the following equation was obtained[144,146]:

$$\frac{\Delta[M]}{[M]} = \frac{1}{g}\exp(gk[I]^{1/2}t - 1) \qquad (12)$$

where $k = k_p k_{in}^{1/2}/k_t^{1/2}$ is a constant, $g = -\{1 + [M]_c/[P]_c - v_c[M]_c/v_d[P]_c\}$ is an acceleration factor characterising the autocatalytic effect (the subscripts c and d refer to the concentrated and dilute phases respectively, and v is the

rate of polymerisation. When the exponential function is expanded as a series, we obtain

$$\frac{\Delta[M]}{[M]} = \frac{1}{g}\left\{gk[I]^{1/2}t + \frac{g^2k^2}{2!}([I]^{1/2}t)^2 + \frac{g^3k^3}{3!}([I]^{1/2}t)^3 + \ldots\right\} \quad (13)$$

Eqn. (13) accounts for the higher (more than 0.5) order of the reaction with respect to the initiator. The agreement between the experimental data and the theoretical curve calculated by Eqn. (12) is fairly satisfactory for vinyl chloride up to 50—60% conversion (polymerisation temperature 50°C, initiators—benzoyl and lauroyl peroxides and azobisisobutyronitrile)[146]. Russo et al.[147] used this hypothesis as a basis for a kinetic mechanism of radiation-induced polymerisation of vinyl chloride.

Among the available models, that described above gives perhaps the most accurate description of the quantitative aspect of the kinetics of heterophase polymerisation of vinyl chloride. It postulates the proportionality of the rate of reaction to the weight of the polymer formed and is also confirmed by Bort's data[114] concerning the existence of a solution of poly(vinyl chloride) in the monomer. However, it is still not clear to what extent it is applicable to the polymerisation of acrylonitrile, where the solubility of the polymer in the monomer is much lower than in the poly(vinyl chloride)—vinyl chloride system.

Of the kinetic mechanisms giving a clear and correct description of the physical and chemical processes occurring in heterophase polymerisation, we shall also mention Dainton's mechanism[82,83] proposed for the polymerisation of acrylonitrile in water. It includes reactions in the liquid and solid phases and takes into account interfacial processes—the aggregation of macromolecules and primary polymer particles (microglobules), the "trapping" of the radicals from the liquid phase, chain termination reactions at the interfaces between the phases and within the phases, and adsorption of monomer molecules by polymer particles.

A. Reactions in the liquid phase. 1. Initiation $I \rightarrow 2R_1^{\cdot}$. 2. Chain propagation $R^{\cdot} + M_{aq} \rightarrow R^{\cdot}$. 3. Chain termination $R^{\cdot} + R^{\cdot} \rightarrow P$.

B. Processes in the polymer phase. 1. Conversion of the critical particles p into primary polymer particles P:

$$p + p \rightarrow P$$

and

$$p + P \rightarrow P\ .$$

2. Slow aggregation of the primary particles:

$$\begin{matrix} P + P \rightarrow P \\ P + P^{\cdot} \rightarrow P^{\cdot} \end{matrix}$$

3. Particle growth:

$$P^{\cdot} + M_a \rightarrow P^{\cdot}\ .$$

C. Interfacial processes. 1. Weak adsorption of the monomer by polymer particles $M_{aq} \rightarrow M_a$. 2. Activation of the particles—trapping of radicals by polymer particles:

$$R^{\cdot} + P \rightarrow P^{\cdot}\ .$$

3. Chain termination by radicals from different phases:

$$R^{\cdot} + P^{\cdot} \rightarrow P\ .$$

Kiuchi et al.[148] were able to relate the concentration of the adsorbed monomer (acrylonitrile) $[M]_a$ to its concentration in the aqueous phase $[M]_{aq}$:

$$[M]_a = \frac{\beta}{V_e^{0.5}}[M]_{aq}^2\ , \quad (14)$$

where β is a coefficient varying with the dimensions and the physical state of the polymer particles and V_e is the effective volume of the reactant.

4. The Emulsion Polymerisation Model

Some investigators[10,11] stress the similarity of the systems under consideration, particularly of polymerisation in an aqueous medium, to typical emulsion polymerisation systems. This analogy is based on the morphological and kinetic characteristics of both processes—self acceleration, high average rates and high molecular weights of the polymers, globular nature of the particles, etc. In both cases, the number of polymer particles remains constant in the course of polymerisation. In heterophase polymerisation, the number of particles per cm^3 of the medium is 10^{12}—10^{14}, which is the lower limit in emulsion polymerisation. The monomer consumed in the growing polymer particles is constantly replenished, as in emulsion polymerisation, by diffusion of the monomer molecules from the liquid phase.

Thomas and Webb[150], who employed emulsion polymerisation as a model, calculated k_p from the rate of polymerisation of acrylonitrile in water. The resulting value $k_p = 2 \times 10^4$ litre $mole^{-1}$ s^{-1} agrees satisfactorily with Dainton's data[82,83].

Kiuchi et al.[149] concluded that the principal centres of heterophase polymerisation of acrylonitrile are polymer particles, as in emulsion polymerisation. However, it was found that the relation between the rate of polymerisation and the number of particles is much less pronounced than in typical emulsion polymerisation. The authors explain this difference by the fact that in the first case the heterogeneity of the system due to the insolubility of polyacrylonitrile in the monomer allows each polymer particle to contain more than one radical and therefore it cannot be regarded as an independent centre of propagation of the reaction.

Recently a kinetic mechanism, based on the Smith—Ewart theory was proposed[151] (polymerisation of methyl methacrylate in water). It was suggested that chain propagation takes place on the surface of the particles, the number of which remains constant after the coalescence of the macromolecules. Then

$$v = k_p\frac{\bar{n}N}{N_A}[M]_a, \quad (15)$$

where N is the number of particles, $\bar{n}$ the average number of radicals per particle (proportional to the surface area of the particle or its volume raised to the power 2/3), N_A the Avogadro number, and $[M]_a$ the concentration of methyl methacrylate in the polymer particle assuming it to be proportional to its concentration in the aqueous phase, i.e. $[M]_a = k_1[M]_{aq}$.

After rearrangement, we obtain

$$v = k_p k_1 V_p^{2/3}\frac{N^{1/3}[M]_{aq}}{N_a}\ , \quad (16)$$

where V_p is the overall volume of the polymer phase. It follows from Eqn. (16) that the rate of polymerisation is proportional to the number of particles raised to the power 1/3 and to the concentration of the monomer raised to the power 5/3. Experimental data agree satisfactorily with these conclusions.

5. Theory of Monomolecular Chain Termination. Other Theories.

According to the theory of Thomas and Pellon[12], the occlusion of certain macroradicals can reach such an extent that they become incapable of chain propagation and bimolecular chain termination reactions. This effect resembles the monomolecular chain termination reactions. Thus one may assume that radicals are destroyed via bi- and mono-molecular reactions:

$$-\frac{d[R^{\cdot}]}{dt} = k_t[R^{\cdot}]^2 + k_t'[R^{\cdot}]$$

Having postulated a steady state, the authors obtained an equation for the polymerisation of acrylonitrile in bulk:

$$v = (A^2 + B[I])^{1/2} - A \qquad (17)$$

where

$$A = \frac{k_t'k_t[M]}{2k_t}; \quad B = \frac{k_{in}(k_p[M])^2}{k_t}.$$

Eqn. (17) agrees with experimental data up to 50% conversion of the monomer. Bamford and Jenkins[6] criticised the theory of monomolecular chain termination on the grounds that, for the theory to be valid, the concentration of blocked radicals must be much higher than that of the "trapped" radicals found experimentally.

Durup and Magat[152] suggested that, when the degree of blocking of the macroradicals is a maximum, chain termination is due solely to the primary radicals. However, this hypothesis fails because post-polymerisation takes place at a decreasing rate despite the removal of the source of primary radicals.

Schindler and Breitenbach's analysis[153] of kinetic data for the polymerisation of vinyl chloride is based on the relation which the authors found between the decrease of the chain termination constant owing to the occlusion of free radicals and conversion:

$$k_t = \frac{k_{ti}}{(1 + k^*C)^{1/2}}, \qquad (18)$$

where C is the conversion, k_{ti} the constant for the initial rate of termination, and $k^* = 50$ is a dimensionless constant.

It was established that, up to 20% conversion at 50°C, the following equation holds:

$$C = \frac{k^*v_i^2}{4}t^2 + v_i t \qquad (19)$$

where v_i is the initial rate of polymerisation. This expression is analogous to Eqn. (13) to within the second term.

However, Cotman et al.[49] showed that the constant k^* depends on the rate of polymerisation and tends to increase with the increase of the initial rates of polymerisation. A deficiency of the kinetic equations (17)—(19) is their empirical nature and hence limited applicability.

Magat[154] examined the quantitative aspect of the polymerisation of vinyl chloride. He believed that a steady state is not attained by the system for a long time owing to the low rate of chain termination. Thus self acceleration is caused by the increase in the concentration of macroradicals during the reaction. Despite the fact that the results for vinyl chloride agree satisfactorily with the experimental data, the equation obtained for a non-steady state is inapplicable to the polymerisation of acrylonitrile and vinylidene chloride[154].

If the polymer is capable of crystallising, the kinetic mechanism is complicated still further, since it is then necessary to take into account the differences between the rate constants for the elementary reactions involving the crystalline and amorphous phases[17,155]. The kinetics of heterophase polymerisation can be influenced also by the different reactions of the radicals, as shown for polyethylene[106,156].

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One may suppose that further advances in the field of heterophase polymerisation will be achieved by studying both chemical and physical processes accompanying the formation of the polymer phase, in particular by studying different chemical reaction in such systems, the morphological structure and swelling of the polymer particles, the adsorption and diffusion of monomer molecules in the particles, the ratio of the concentrations of the monomer in the liquid and solid phases, etc.

ADDENDUM

Quite recently a number of studies were published on the kinetics and mechanism of heterophase polymerisation and copolymerisation[157-164]. Among these, an investigation[157] where the kinetics of the polymerisation of vinyl chloride in bulk were interpreted qualitatively and quantitatively on the basis of the two-phase theory, is of interest. It is noted that the polymer phase consists of particles swollen in the monomer, the composition of which remain constant up to about 70% conversion. However, in contrast to the theory developed by Talamini[144], the above theory does not include the hypothesis of a steady distribution of radicals between the two phases corresponding to thermodynamic equilibrium, since owing to sorption processes the concentration of radicals in the polymer particles increases continuously with conversion, which is the reason for the autocatalytic nature of the polymerisation. Quantitative calculations showed that at low conversions the chain propagation and termination reactions already take place preferentially within the particles and the number of radicals in the liquid phase is independent of the rate of their termination. The proposed mechanism accounts for the decreased rate of polymerisation (discussed above) on formation and aggregation of particles as due to the increased rate of termination of radicals within the particles in consequence of the increase of their concentration in the effective volume of the condensed phase; the increase in the initial rate of polymerisation of vinyl chloride in bulk and the decrease of self acceleration following the introduction of chain transfer agents[33,34] are explained by the increase of the rate of liberation (desorption) of radicals into the liquid phase.

The kinetic data[158] obtained for the polymerisation of vinyl chloride in bulk (weak post-polymerisation at 25°C, low radical concentration, and a reaction order close to 0.5 with respect to intensity of irradiation) can also be interpreted satisfactorily on the basis of the two-phase model.

Thus, despite their somewhat limited applicability to different monomers, some of the theories discussed (the occlusion and two-phase theories) permit a satisfactory explanation of many characteristics of heterophase polymerisation.

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Institute of Chemical
Physics, USSR
Academy of Sciences,
Moscow

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Electrode Behaviour of a Suspension of Insoluble Material

M.R.Dausheva and O.A.Songina

The electrochemical behaviour of suspensions of insoluble materials at different electrodes is discussed, with special emphasis on recent studies of the adhesion of particles of a suspension to the surface of the dropping mercury electrode and of the rotating amalgamated disk electrode. 89 references.

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I. INTRODUCTION

Processes in which electron transfer involves insoluble materials (in addition to the electrode metal and the electrolyte) have recently attracted a great deal of attention among electrochemists. We can distinguish three separate cases[1]:

1. The electrode is made of an insoluble compound (single crystal, pressed powder, solidified melt); electron transfer takes place between the electrolyte and the insoluble substance.

2. A metallic electrode is covered with a film of an insoluble substance (for example, an oxide film); in this case electron transfer takes place between the electrolyte, the insoluble substance, and the electrode metal.

3. The insoluble substance is present in suspension in the electrolyte; electron transfer between the insoluble substance and the electrolyte can occur either directly or through dissociation of the substance into electrochemically active ions.

Cases 1 and 2 have been fully investigated in theoretical electrochemistry, and are widely used in practice (for example, in accumulators, cells, and rectifiers). On the other hand, relatively little work has been done on the electrochemical behaviour of suspensions (case 3), largely because of the difficulties arising in studies of heterogeneous systems. If these difficulties could be overcome, new prospects would be created in theoretical and in applied electrochemistry. This review attempts to systematise existing data on the electrochemical behaviour of suspensions.

II. MECHANISMS OF ELECTROCHEMICAL REACTIONS INVOLVING SUSPENSIONS

Most of the published papers on the electrochemical behaviour of suspensions† relate to their reduction. We shall therefore discuss the mechanisms by which suspensions can be electrochemically reduced. However, the same mechanisms can be invoked, in general, for the oxidation of suspensions.

The following mechanisms are possible for the electrode reactions of suspensions.

Mechanism I is an electronic mechanism, involving direct discharge of the solid particle

for salts

$$[M^{n+} + n\,A^-] + ne \rightarrow M + n\,A^- \qquad (1)$$

for oxides

$$\left[M^{n+} + \frac{n}{2}\,O^{2-}\right] + ne + \frac{n}{2}\,H^+ \rightarrow M + \frac{n}{2}\,OH^- \qquad (1')$$

In the case of reduction of oxides the process has been termed[2] electronic–protonic.

Eqns. (1) and (1′) give only a very general description of the process. The detailed discussions of reduction processes found in the literature on oxide electrodes are beyond the scope of the present review. However, we can state that the mechanisms considered for oxide electrodes[2,3] are also applicable, in general, to the discharge of particles of a suspension in contact with the electrode surface.

Mechanism II. An intermediate (X) formed at the electrode during the process takes part in the electron transfer:

for salts

$$[M^{n+} + n\,A^-] + n\,X \rightarrow M + n\,X^+ + n\,A^- \qquad (2)$$

for oxides

$$\left[M^{n+} + \frac{n}{2}\,O^{2-}\right] + n\,X + n\,H^+ \rightarrow M + n\,X^+ + \frac{n}{2}\,H_2O \qquad (2')$$

Mechanism III. The particle of insoluble substance decomposes into ions; the metal ions or the anions are discharged at the electrode:

for salts

$$[M^{n+} + n\,A^-] \rightarrow M^{n+} + n\,A^- \qquad (3)$$

for oxides

$$\left[M^{n+} + \frac{n}{2}\,O^{2-}\right] + n\,H^+ \rightarrow M^{n+} + \frac{n}{2}\,H_2O \qquad (3')$$

$$M^{n+} + ne \rightarrow M \qquad (3'')$$

† The term "suspension" is used to denote unstable, coarsely dispersed systems (particle size $\gg 1\ \mu m$), in contrast to colloids which are stable for very long periods.

Evidently, the decomposition of the particles into ions is determined (for an insoluble substance) by the solubility product of the compound and by the nature of the electrolyte.

Thus, direct electrochemical discharge of an insoluble substance at an electrode occurs only by mechanism I.

It is often difficult to identify the discharge mechanism for the particles of a suspension, and as a result different interpretations of a given process are sometimes found. Thus, the debate on the mechanism of reduction of manganese and tungsten oxide suspensions is well known[4-7]. Kobozev[4,5] states that tungstic oxide is reduced by free hydrogen atoms when hydrogen is evolved at a high-overvoltage cathode (such as lead); on a low-overvoltage (platinum) cathode the reduction involves excited hydrogen molecules (mechanism II). According to Kobozev, manganese dioxide is not reduced at either cathode in spite of its good electrical conductivity. Bagotskii and coworkers[6], and also Lukovtsev[7], prefer mechanism I, and state that tungsten trioxide and manganese dioxide are reduced at high-overvoltage cathodes (mercury, or amalgamated copper) without involving any form of active hydrogen whatsoever: by direct electron transfer, or (in the case of manganese dioxide) by interaction with the mercury of the electrode.

The difficulty of identifying the electrochemical reaction mechanism of a suspension stems from the large number of factors which can influence the electrochemical reduction or oxidation of a suspension: electrode material, electrolyte composition, current density, electrical conductivity of the solid phase, solubility product of the suspended phase, the contact between the solid phase and the electrode, etc.[3,8-11].

It is usually assumed that an electronic discharge mechanism must be involved in the reduction of compounds possessing an appreciable electrical conductivity (10^{-2}–10^{-5} ohm^{-1} cm^{-1}). Poor conductors, on the other hand, are reduced by mechanisms II and III. Evidently, depending on the electrolysis conditions, the process can occur by several mechanisms, but one mechanism usually predominates. For example, the decomposition of particles of an insoluble substance (mechanism III) is accompanied to a greater or lesser extent, depending on the solubility product and on the nature of the electrolyte, by processes which involve the first two mechanisms.

III. BEHAVIOUR OF SUSPENSIONS OF INSOLUBLE SUBSTANCES DURING ELECTROLYSIS

Most of the work on the electrolysis of suspensions has been concerned with their reduction on platinum electrodes. The first publication on this topic was due to Fischbeck[12], who studied the reduction of powdered metal oxides, sulphides, and halides at a platinum cathode in sulphuric acid solutions. Many workers have shown[13-21] that silver halides are easily reduced at a platinum electrode, the silver being deposited on the cathode as a metallic sponge with a very good current yield. The reduction of silver chloride occurs mainly in the solid phase[14-18], i.e. by mechanism I; however, mechanism III can occur at low current densities[8]. Suspensions of lead halides are also easily reduced[14-21]. In a potassium chloride solution they are reduced by direct electron transfer from the electrode (mechanism I), but Sancelme[22] suggests that atomic hydrogen is involved in the reduction of lead halides (mechanism II).

The medium plays a very important role in the reduction of suspensions. Cupric oxide, cuprous oxide, and copper hydroxide are fully reduced to metallic copper only in sufficiently acid solutions. In dilute acids, and also in alkalis, the reduction is slow and does not go beyond a mixture of metallic copper and cuprous oxide[8,10]. Evidently, reduction in acid solutions is assisted by partial dissolution of the oxides (mechanism III). Lead sulphate[19,21] is not easily reduced at a platinum electrode in dilute neutral solutions, and is entirely unaffected in solutions of sulphuric acid. This is thought to be due to the poor electrical conductivity of lead sulphate; furthermore, the dissociation of lead sulphate into ions is hindered in sulphuric acid solutions, and reduction by mechanism III is impossible. Thus, lead sulphate is easily reduced in solutions of hydrochloric acid, sodium carbonate, and sodium hydroxide in which it is partly soluble. Lead phosphate, chlorophosphate, and chromate also can be reduced only in electrolytes in which they are appreciably soluble[19]. Vanadium pentoxide is smoothly reduced to vanadium in dilute sulphuric acid solutions[22]. The hydroxides of tervalent iron and nickel[23] are reduced to the hydroxides of the bivalent metals in neutral solutions. A suspension of α-Fe_2O_3 is reduced to the metal in a concentrated sodium chloride solution, mainly by the action of atomic hydrogen but with a contribution by the electronic mechanism[24].

Platinum is not the only electrode metal on which the reduction of suspensions of insoluble compounds has been investigated. As stated above, some workers have used a mercury cathode[7] and cathodes of amalgamated lead[5] and copper[7]. The reduction of lead, copper, cadmium, zinc, and titanium oxides at a lead cathode has also been studied[25]. A lead cathode has been used to reduce the sulphides and other salts of various metals[26,27]; a silver cathode has been used to reduce a suspension of silver suboxide[28]. Vrebosch and Tiggelen[20] studied the reduction of silver halides and of copper sulphide suspended in dilute solutions of sodium chloride and sulphuric acid, using silver and copper electrodes respectively. It can be seen from the "potential–time" curves for a mixture of silver chloride, bromide, and iodide that the processes corresponding to the reduction of each halide can be resolved in time[20]. The reduction of copper sulphide at a copper electrode in dilute sulphuric acid goes as far as metallic copper, and is accompanied by the evolution of hydrogen and hydrogen sulphide[20]. The reduction of a suspension of cupric and cuprous oxide[8] at a copper cathode in 0.1 *N* sodium hydroxide proceeds mainly by direct electron transfer:

$$CuO + 2e \rightarrow Cu + O^{2-} \quad (4)$$

$$Cu_2O + 2e \rightarrow 2Cu + O^{2-} \quad (4')$$

$$O^{2-} + H_2O \rightarrow 2OH^- \quad (4'')$$

The reduction of cupric and cuprous oxide begins at potentials more negative than the theoretical values by 338 and 616 mV respectively, indicating the presence of a slow step (overvoltage). The authors[8] suggest that reduction by hydrogen adsorbed on the electrode also occurs, but to a smaller extent:

$$H_2O + M + e \rightarrow MH_{ads} + OH^- \quad (5)$$

$$CuO + 2MH_{ads} \rightarrow Cu + H_2O + 2M \quad (5')$$

The symbol M denotes the electrode metal.

The reduction of cupric hydroxide on a copper cathode is attended by a very large overvoltage, and occurs at a

potential 954 mV more negative than the theoretical value[8]. It is concluded that the reduction of cupric hydroxide has a greater dependence on the participation of adsorbed hydrogen than does the reduction of the copper oxides:

$$Cu(OH)_2 + 2MH_{ads} \rightarrow Cu + 2H_2O + 2M \quad (6)$$

With the hydroxide, however, dissociation is possible, and the reaction proceeds partially through the reduction of copper ions:

$$Cu(OH)_2 \rightarrow Cu^{2+} + 2OH^- \quad (6')$$

$$Cu^{2+} + 2e \rightarrow Cu \quad (6'')$$

In the above examples the intermediate (X) which is formed at the electrode and reacts chemically with the insoluble substance is hydrogen. However, this role can be played by other substances, for example metal ions which can exist in two valency states. Addition of such ions to the electrolyte is suggested[29] as a means of increasing the rate of the electrochemical reduction of suspensions of insoluble compounds. For example, suspensions of bismuth oxide and cuprous chloride are reduced electrolytically at a lead cathode in the presence of quadrivalent titanium:

$$Ti^{4+} + e \rightarrow Ti^{3+} \quad (7)$$

$$Bi_2O_3 + 6Ti^{3+} + 6H^+ \rightarrow 2Bi + 6Ti^{4+} + 3H_2O \quad (7')$$

$$CuCl + Ti^{3+} + H^+ \rightarrow Cu + Ti^{4+} + HCl \quad (7'')$$

Some electrochemical studies of the anodic oxidation of suspensions have also been reported. A suspension of arsenious oxide is oxidised to arsenic acid[30]; manganous hydroxide, formed by mixing solutions of manganous sulphate and ammonia, is oxidised to manganese dioxide at an iron anode[31]; manganous carbonate in a sodium chloride solution is also oxidised to manganese dioxide[32]. The oxidation of suspensions of bivalent nickel and cobalt hydroxides and of lead oxide on graphite in sodium chloride solutions[29] involves the chlorine formed at the anode, and the oxidation products are tervalent nickel and cobalt hydroxides and lead dioxide.

Only a few individual papers have dealt with the practical applications of the electrolysis of suspensions. The process has been used as a preparative method for manganese dioxide[31,32], and to convert sparingly soluble compounds into a soluble form[10,22]. The work[33-35] on the production of pure metals directly from their ores could have great practical importance. One of these papers[35] deals with the electrochemical "extraction" of lead compounds. The lead ore, suspended in a chlorate solution, is introduced into the anode compartment of the electrolytic cell and vigorously stirred throughout the reaction. The lead gradually goes into solution, is transferred to the cathode compartment, and is deposited as a sponge on the lead cathode in 86–90% yield. Electrolysis of a suspension of galena in a mixed melt of potassium and sodium chloride yields[33,34] the metal at the (molten lead) cathode and sulphur at the anode. A technical process for the continuous electrolysis of lead concentrates in fused salts could be based on this experiment. The yield of lead is 96–97%, and the purity of the deposited metal is 99.8–99.9%.

Several workers[36-38] have begun to use the suspended electrode method for studies of catalysts. A conventional electrode of the pressed catalyst acts as a current carrier and a carrier of catalytic activity at the same time: by using a suspension of the catalyst these two functions can be separated. The method has been used to study the anodic behaviour of a suspension of Raney-nickel in a sodium hydroxide solution on platinum and gold electrodes, and the cathodic behaviour of a suspension of aluminium oxide (carrier) with additions of silver (catalyst).[36] When the catalyst contacts the electrode, hydrogen is oxidised in the anodic process and oxygen is reduced in the cathodic process. The method has been recommended for studying the oxidation of organic compounds in fuel cells[36]. The electrolytic oxidation of hydrogen and methanol has been studied[37] by the suspended electrode method, using suspensions of platinised and nickel-coated carbon, and Raney-nickel. The effectiveness of catalysts for the porous diffusion electrode of a fuel cell[38] has been assessed by using suspended electrodes of platinum black and Adams' catalyst (finely divided PtO_2). With these suspended electrodes the material in suspension does not react electrochemically at the electrode, and therefore work in this area falls outside the scope of the present review.

Suspensions of sparingly soluble compounds can be reduced by cementation with liquid amalgams[39-41] as well as by electrolysis. When a suspension is stirred with an amalgam the metal from the compound in suspension goes into the mercury, from which it can be extracted by shaking the resulting amalgam with a solution of mercurous nitrate. The liquid amalgam can be brought into intimate contact with the particles, and the electrochemical reaction is therefore favoured. The cementation reaction, which takes place at high negative mixed potentials, is accompanied by hydrogen evolution. Hence, there is a possibility that the reduction of suspensions of sparingly soluble compounds by cementation with amalgams will occur by mechanism II (with participation of the evolved hydrogen) as well as by an electronic mechanism. It has been shown[40] that the behaviour of suspensions in this respect is fully consistent with the electrochemical theory of cementation processes[42]. The cementation method is used mainly to separate precipitates and to convert insoluble into soluble compounds. Thus, cementation with zinc amalgam[39] has been used analytically to separate lead sulphate quantitatively from barium sulphate, and cementation with sodium amalgam has been used to bring into solution heavy metal chlorides, sulphates[40], and carbonates[41].

IV. ELECTROCHEMICAL BEHAVIOUR OF SUSPENSIONS ON SOLID MICRO-ELECTRODES UNDER AMPEROMETRIC TITRATION CONDITIONS

The reduction or oxidation of insoluble substances at an electrode is often encountered in amperometric titrations by the precipitation method[43-51]. The precipitate formed during the titration is sometimes reduced or oxidised at the platinum microelectrode either directly (by contact between the particles and the electrode) or by partial dissolution of the precipitate (if its solubility product is not too small). As a result, the equivalence point on the titration curves becomes ill-defined, and precision is lost. Because of this problem, special electrochemical studies of suspended precipitates with platinum microelectrodes have been undertaken.

Songina and Zakharov[43] made a detailed study of the reduction and oxidation of mercuric iodide precipitates in 1 M sulphuric acid. The oxidation and reduction polarograms of mercury iodide show clearly defined limiting current plateaux: the reduction begins at +0.3 V and the

oxidation at +1.0 V (relative to the mercury/iodide electrode). Because of the very low solubility product of mercuric iodide (5×10^{-29}), it has been suggested that the reduction and oxidation of this compound proceed by the electronic mechanism

$$HgI_2 + 2e \rightarrow Hg + 2I^- \quad (8)$$

$$HgI_2 - 2e \rightarrow Hg^{2+} + I_2 \quad (8')$$

By comparing the polarograms for the reduction of mercuric ions and for the oxidation of iodide ions with those for the oxidation and reduction of a suspension of mercuric iodide it can be shown that the reduction potential of the suspension is 0.4 V more negative, and the oxidation potential 0.4 V more positive, than the corresponding potentials for the mercuric and iodide ions respectively. It is concluded that sharp titration curves can be obtained by carefully setting the potential at a value where neither oxidation nor reduction of the precipitate can occur.

Detailed studies have been reported also of the reduction of silver halide[45-47] and of silver and mercury molybdate and tungstate suspensions[48-51].

The reduction of a sparingly soluble precipitate of silver chloride was used as the basis of an original method for the amperometric titration of iodide in the presence of chloride by a solution of silver nitrate[52]. Particles of silver chloride are formed after the end-point of the titration of the iodide ions: their reduction (at a graphite electrode maintained at a potential of +0.38 V relative to another graphite electrode coated with silver) produces a sharp increase in current.

V. ELECTROCHEMICAL BEHAVIOUR OF SUSPENSIONS ON MERCURY MICRO-ELECTRODES

Micka and Kalvoda's papers on the reduction of suspensions of sparingly soluble compounds (termed "insoluble depolarisers") by classical[53-55] and by oscillographic polarographic methods[56,57] began to appear in the 1950's. Micka used a dropping mercury electrode and conventional polarographic base electrolytes (solutions of sulphuric acid, salts, etc.). The polarograms of his stirred suspensions usually showed a current step over a well defined potential region[53,55], accompanied by sharp current fluctuations associated with the irregular collisions of the solid particles against the electrode (Fig. 1). At more negative potentials the current falls back to the background value. The polarogram plotted without stirring is indistinguishable from the polarogram for the base electrolyte, because the precipitate settles and cannot contact the dropping mercury electrode. The peak height and the frequency of the current fluctuations increase with the rate of stirring and with the number of solid particles in suspension. Micka examined suspensions of several dozen sparingly soluble compounds (sulphides, oxides, chlorides, elemental sulphur, etc.[55]), and determined the potentials corresponding to the maxima in their reduction polarograms.

Kalvoda studied the reduction of suspensions by Heyrovsky and Foreit's oscillographic polarography method[56,57]. He plotted $dE/dt = f(E)$ curves for single-sweep and repeated-sweep polarisations of the dropping electrode. Lobes were found in the oscillograms (Fig. 2) at potentials close to those of the maxima obtained by Micka using classical polarography[55]. By comparing the oscillograms given by single-sweep and multiple-sweep polarisations, Kalvoda concluded that in many cases the direct reduction of solid particles is accompanied by reactions involving the products of interactions between the particles and the electrolyte. For example, suspensions of sulphides and elemental sulphur in acid solutions give an additional peak on the polarogram, corresponding to electronic processes involving the SH^- ions formed at the electrode, and the oscillograms of many substances show additional peaks due to the reduction of metal ions produced by the partial dissolution of the solid particles or to chemical reaction of the sulphide with mercury ions produced by dissolution of the mercury electrode under anodic polarisation:

$$MS + Hg^{2+} \rightarrow M^{2+} + HgS \quad (9)$$

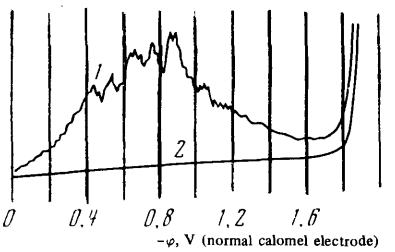


Figure 1. Polarograms obtained with a carbon suspension (20 mg) in a 1 M NH_4Cl base electrolyte (5 ml) using a dropping mercury electrode: 1) stirred, 2) unstirred (from Ref. 53).

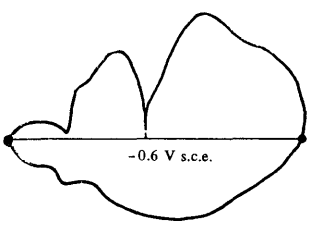


Figure 2. Oscillographic polarogram of a suspension of AgI in 0.5 M KCl, measured with a dropping mercury electrode[56].

Kalvoda points out that the electrochemical behaviour of suspensions of sparingly soluble compounds can be predicted from a knowledge of the position of the metallic component in the electrochemical series: the more noble the metal, the more easily are its sparingly soluble compounds reduced. For example, suspensions of copper, mercury, silver, etc. compounds are easily reduced. Conversely, suspensions of the insoluble compounds of metals such as calcium and magnesium are not reduced at all.

Micka made a detailed study[54,58] of the reduction at a dropping mercury electrode of suspensions of sulphides

of the iron-group metals (Fe_2S_3, FeS, CoS, NiS). The reduction polarograms obtained in the presence of ammonium salts have a sharp current maximum (peak) at potentials 1.5–1.7 V more negative than the normal calomel electrode. The following mechanism is proposed[54,58]:

$$MS + 2e \rightarrow M + S^{2-} \quad (10)$$

$$S^{2-} + 2\,NH_4^+ \rightarrow H_2S + 2NH_3 \quad (10')$$

$$M + H_2S \rightarrow MS + H_2 \quad (10'')$$

There are serious objections to this mechanism, since reactions (10′) and (10″) are impossible under these conditions. Firstly, the reaction between sulphide ions and ammonium ions in aqueous solution should lead to the formation of ammonium sulphide: this, being the salt of a weak acid and a weak base, should be almost completely hydrolysed with formation of SH^- ions and ammonium hydroxide. Secondly, it is hard to accept the oxidation of a metal on the surface of the electrode at a fairly negative potential by hydrogen ions from hydrogen sulphide. Alternative mechanisms, suggested by Micka, seem more convincing: 1) since metals of the iron group are insoluble in mercury, the metal atoms formed by reaction (10) do not penetrate into the mercury but remain on the electrode surface, and the reduction of hydrogen takes place on the metal rather than on mercury, i.e. at a lower overvoltage; 2) as a result of the relatively high electrical conductivity of the heavy metal sulphides the particles of the suspension acquire the potential of the electrode when they collide with its surface, and the hydrogen is reduced at a lower overvoltage.

The catalytic evolution of hydrogen at a dropping mercury electrode in the presence of suspensions of semiconductors‡ was studied by Japanese workers[59] in a 1 M NH_4Cl base electrolyte. The aim of this work was to correlate the properties of the semiconductor (Si, Ge, P, As, Sb, CdSb, CdTe, Sb_2S_3, ZnS, Bi, S, Se, Te, PbS, Bi_2Te_3, InAs) with the shape of the polarogram. As with the sulphides of the iron group[54], the polarograms of suspensions of semiconductor catalysts have a current maximum at a potential more negative than −1.0 V. The height of the maximum depends on the electrophysical properties of the semiconductor and on the concentration of the suspension. The potential of the maximum depends on the width of the forbidden gap of the semiconductor. Electrolysis on the macro scale has shown[59] that a semiconductor suspension lowers the overvoltage for hydrogen evolution. A possible mechanism is the following[59]:

$$\underset{\text{on electrode}}{(\text{Catalyst}) + NH_4^+} \rightarrow \underset{\text{on electrode}}{(\text{Catalyst})H^+} + NH_3 \quad (11)$$

$$\underset{\text{on electrode}}{2(\text{Catalyst})H^+} + 2e \rightarrow \underset{\text{on electrode}}{2(\text{Catalyst})} + H_2 \quad (11')$$

The particle itself is not reduced. An analogous mechanism has been proposed[60] for cobalt sulphide. It should be noted, however, that with sulphide suspensions one must consider, in addition to catalytic hydrogen evolution (for sulphides of the iron group[54,60] metals) and to direct reduction of the solid particles of the suspension (for sulphides of metals such as copper, mercury, etc.[55]), also the reduction of the mercury sulphide film formed at the surface of the mercury drop by the sulphide and hydrogen sulphide ions present in these suspensions. The formation and the reduction of such a film in solutions containing S^{2-} and SH^- ions and a suspension of elementary sulphur has been discussed by Kiselev and Zhdanov[61–64].

‡ The term "semiconductor" is used[59] in the wider sense to include electrical insulators.

VI. MECHANISM OF THE ATTACHMENT OF SUSPENDED PARTICLES TO THE ELECTRODE SURFACE

The reduction of insoluble substances at a dropping mercury electrode in a well defined potential region (Fig. 1) is ascribed by Micka to the existence of adsorption forces between the electrode and the solid particles at these potentials[53]. At very negative potentials repulsive forces arise, and the current falls off[65]: this conclusion is reached from the work of Voropaeva and coworkers[66], who measured the repulsive forces between two crossed wires (gold and platinum) in various electrolytes as a function of the potential of the wires, and found that the force is a minimum at a definite potential.

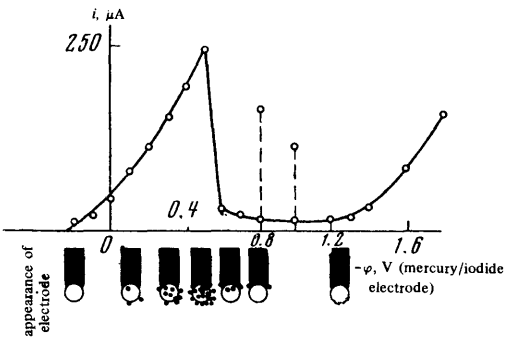


Figure 3. Reduction polarogram of a suspension of Hg_2I_2 (0.01 mole litre^{-1}) in 0.1 M KNO_3, measured[67] with a "hanging mercury drop" electrode and a mercury/iodide reference electrode.

Measurements of the polarographic reduction[67] of insoluble halide and mercury oxide suspensions with a "hanging mercury drop" electrode have shown that an increasing proportion of the particles becomes attached to the electrode surface as the cathodic polarisation is increased to −(0.4–0.5) V relative to the mercury–iodide electrode, but at −(0.5–0.6) V the particles are strongly repelled (Fig. 3). The maximum current in the polarogram corresponds to the maximum number of particles attached to the surface, and the decrease in current corresponds to expulsion of the particles: in other words, the polarographic currents of the suspension are related to the attachment of particles to the electrode surface and to their subsequent reduction. The potential region corresponding to the current maximum extends on either side of the zero-charge potential ($\varphi_{\epsilon=0}$). Electrocapillarity measurements by the mercury drop time method[68] in suspensions of mercury oxides and halides have confirmed that the potential of the current peak is close to the potential of the maximum on the electrocapillarity curve, i.e. to the zero-charge potential.

Jones and Kaye[69] also stressed the significance of $\varphi_{\epsilon=0}$ in their work on the reduction of suspensions of various carbons on mercury-pool and hanging-mercury-drop electrodes. They ascribe the current maximum on the reduction polarograms of their suspensions to the damping of the motion of the mercury surface near the zero-charge potential, which enables the particles to come into contact

with the mercury surface, rather than to attraction of the particles by the surface: as the potential deviates from $\varphi_{\epsilon=0}$ in either direction, the surface of the mercury and the adjacent layer of electrolyte experience violent motions (as in the case of polarographic maxima of the first kind) which destroy the contact between the particles and the surface. However, it is difficult to reconcile this explanation with the absence of a reduction current at high cathodic polarisations even when intensive stirring is applied to increase the frequency of collisions between the particles and the electrode[53,67]. The loss of the contact between the particles of the suspension and the surface of the electrode at potentials well removed from $\varphi_{\epsilon=0}$ has also been pointed out by other workers[70].

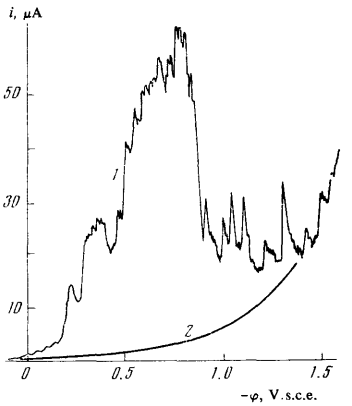


Figure 4. 1) polarogram obtained with a dropping mercury electrode in a suspension of positive oxidised carbon (10 mg) in a 1 M $HClO_4$ base electrolyte (25 ml), deaerated and stirred; 2) polarogram of the base electrolyte (from Ref. 71).

Stirred suspensions of activated oxidised carbons give rise to large polarographic currents, due to the reduction of oxygen-containing surface groups (Fig. 4)[71]. If these suspensions (which are relatively stable, and settle very slowly[72]) are left unstirred, their polarograms lose all the reduction peaks and become identical to the polarogram of the base electrolyte (curves *1* and *2* of Fig. 5). In the presence of molecular oxygen the polarogram develops a reproducible maximum in the region of the oxygen reduction wave at potentials which include the point of zero charge (curve *4* of Fig. 5). The current maximum is due to the reduction of molecular oxygen on the electrode surface, enhanced by the attachment of carbon particles[71,73]. The shape of polarograms for suspensions of active carbons, measured in the presence and in the absence of oxygen, indicates that the particles in unstirred suspensions are not reduced although they adhere to the surface of the electrode at potentials near $\varphi_{\epsilon=0}$. A similar phenomenon was reported by Micka[65], who found that particles at rest on the mercury surface are not reduced.

These phenomena, and the link between $\varphi_{\epsilon=0}$ and the degree of adhesion, are convincingly explained by some observations of Frumkin[74,75] on the relative stabilities of liquid films of different thickness, which are determined by the relationship between the surface tension and the thickness of the layer[74]. When the layer of liquid between a gas bubble and the solid surface is made progressively thinner, a critical thickness is reached beyond which instability sets in. The liquid layer is disrupted, and the bubble can attach itself to the surface, but a very thin film of liquid nevertheless remains between the bubble and the surface. In the case of a metallic surface the adhesion depends on the potential[75]: for example, the attachment of a hydrogen bubble to a mercury surface is instantaneous at the zero-charge potential, because the liquid layer of electrolyte becomes labile in the absence of charge and is easily disrupted by the approaching bubble. As the potential moves away from $\varphi_{\epsilon=0}$ the liquid layers are stabilised by the electrical double layer, and the attachment of the bubbles becomes slower[75]. The surface tension of the layer of electrolyte between the bubble and the electrode (and therefore also the force needed to separate the layer) is proportional to the square of the potential difference between the metal and the solution. Hence, the wettability of the metal by the liquid increases as the potential departs from the point of zero charge, and the angle of contact observed after the attachment of a bubble decreases[76]. The bubble is held in contact with the electrode surface by capillarity forces acting on the perimeter of the area of contact.

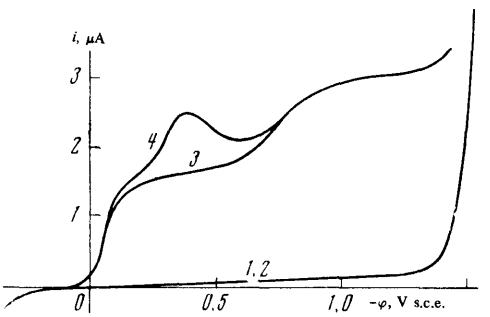


Figure 5. Polarograms measured in 1 M KNO_3 with a dropping mercury electrode: 1) without oxygen or carbon (base electrolyte only), 2) without atmospheric oxygen but in the presence of a suspension of positive oxidised carbon (10 mg in 25 ml); 3) in the presence of atmospheric oxygen but without carbon; 4) in the presence of atmospheric oxygen and a suspension of positive oxidised carbon (10 mg ml^{-1}) (from Ref. 71).

The adhesion phenomenon has been studied also for mercury droplets on glass[77]. The force of attraction between the mercury and the glass surface varies with the potential of the mercury in much the same way as the adhesive force of gas bubbles.

In the case of suspensions, the layer of liquid between particle surface and electrode surface behaves very probably as described above. Thus, the fact that the solid particles become attached to the electrode surface only in a well defined region of potentials can be ascribed to the disruption of labile layers of electrolyte near the zero-charge potential.

By comparing the peak potentials in the polarograms for positive and negative oxidised carbon suspensions[73]

we conclude that the electrostatic effect of the charges on the particles is negligibly small: with a negative carbon the adhesion of the particles reaches a maximum at a charge on the mercury surface slightly more positive (no more than 0.07 V) than with a positive carbon, but the region of adhesion is the same for the two carbons [−(0.3–0.6) V relative to the saturated calomel electrode]. This suggests that the adhesion results primarily from the ready disruption of electrolyte layers in the region of $\varphi_{\epsilon=0}$, rather than from interaction between the charges on the electrode surface and on the particles of the suspension.

In contrast to other types of attachment to an electrode (for example, the interaction of freshly precipitated particles with an electrode, due to the influence of their surface charges), the attachment of particles at potentials close to the point of zero charge may be termed electrocapillary attachment.

The exaltation of the reduction current of dissolved oxygen in the presence of a carbon suspension[71] can be used as a measure of the degree of attachment of the particles to the surface of a dropping mercury electrode as a function of the experimental conditions. The method has been used to demonstrate the dependence of electrocapillary attachment on the amount of carbon in suspension (the "concentration" of the suspension) and on the height of the mercury column (h).[71] By increasing the "concentration" of the suspension we can increase the number of particles attached to the electrode surface, and thus obtain enhanced reduction currents of dissolved oxygen in the potential region which favours attachment of the particles. However, since the drop has a limited surface area, there is a critical "concentration" beyond which further increase has no effect on the oxygen reduction current. The dependence of electrocapillary attachment on h has the characteristic form of slow adsorption processes, in which the maximum in the first oxygen wave is suppressed. This dependence also can be easily explained by invoking the analogy between the adhesion of bubbles and the adhesion of solid particles to the electrode surface. For a bubble of a given size we can define an "induction period": the time for the disruption of the layer of electrolyte between the bubble and the electrode surface immediately before the bubble becomes attached[75]. Evidently, this definition applies also to the particles of a suspension. For low values of h the life time of the drop (τ) is greater than the "induction period", and particles can adhere to the surface of the drop until the drop becomes detached. As h increases the drop time of the mercury decreases, and only those particles whose size corresponds to an "induction period" smaller than τ can become attached. Lastly, at large values of h attachment is impossible because τ is smaller than the "induction period" of even the smallest particles.

Decreasing the concentration of the base electrolyte increases the exaltation of the oxygen reduction current in the presence of a carbon suspension, i.e. it increases the electrocapillary attachment of the carbon particles to the electrode[73]. This effect arises from the increased diffuseness of the double layer, i.e. from the increased double layer thickness: theory predicts[75] that under these conditions the stability of the layers of electrolyte adjacent to the electrode should decrease, and hence the attachment of particles should be enhanced.

Assuming (by analogy with the case of a bubble) that a very thin layer of electrolyte remains between the electrode surface and the particle attached to it, it is easy to see why adsorbed oxygen in unstirred carbon suspensions is not reduced at the electrode (see curve *2* of Fig. 5), in spite of the attachment of particles to the electrode[71]. When the suspension is stirred, however, the layers of electrolyte between electrode and attached particles become even thinner, and may disappear completely, thus allowing the reduction of the oxygen bound to the carbon (see Fig. 4). Frumkin has pointed out[74] that stable layers can become unstable under the influence of quite small external disturbances. If we assume that even the thinnest layers of electrolyte can prevent the reduction of a solid particle at the electrode, we must conclude (from the fact that large currents are observed in stirred but not in unstirred suspensions) that neither the complete disruption of the electrolyte film nor the direct reduction of a particle can be excluded in the case of stirred suspensions.

At potentials too negative to permit electrocapillary attachment the reduction of solid particles of polarographically active suspensions such as mercury halides is suppressed even with vigorous stirring, in spite of the collisions between the particles and the electrode[67]. However, for small negative excursions from the region of attachment potentials [−(0.7–0.9) V s.c.e.] the particles colliding with the electrode squeeze the layer of electrolyte adjacent to the electrode to a very small thickness, or even disrupt it completely, and can be reduced without attachment. Hence, on stirring, the potential region where reduction can occur is shifted towards values more negative than the region of electrocapillary attachment [−(0.3–0.6) V]. For example, a carbon suspension in a neutral base electrolyte gives a current peak at −0.8 V when stirred. In the light of this discussion, the high negative peak potentials observed in the reduction polarograms of other insoluble substances[55] should cause no surprise. Some of the more energetic particles can "puncture" the layer of electrolyte at still more negative potentials, as shown by the sharp and random current surges observed in the polarogram[67].

Summing up, the behaviour of suspensions of insoluble substances at a dropping mercury electrode may be described by the following steps: 1) breakdown of the layer of electrolyte adjacent to the electrode as the particle approaches the surface; 2) attachment of the particle to the electrode surface under the influence of capillarity forces; 3) discharge of the solid particle at the electrode.

As shown above, the second step may be absent, and discharge without attachment can occur if the particle collides with the electrode surface with sufficient energy to disrupt the boundary layer of electrolyte. The third step also is not invariably observed, but only occurs at sufficiently negative potentials.

It is interesting to note that freshly precipitated iron, cobalt, and nickel sulphides (in the form of a very slight turbidity) are not polarographically active[54]. A reduction current appears only when the colloidal sulphide begins to coagulate, i.e. when the particles begin to grow. The lack of electrochemical activity of a freshly precipitated compound (silver bromide) was pointed out also by Bowers and Kolthoff[78]. Most probably, particles of typically colloidal dimensions ($0.1 < r < 1\ \mu m$) such as those of a freshly formed turbidity cannot become attached to the electrode and be reduced because their kinetic energy is insufficient to overcome the disjoining influence of the layer adjacent to the electrode surface. (Deryagin[79] discusses the relationship between the size of colloidal particles and the repulsive forces acting on the particles. It may be assumed that the size of the particle influences also its interaction with the electrode surface.) Reduction currents at a dropping mercury electrode are sometimes

observed in colloidal systems, but they are not usually associated with the direct reduction of the particles. For example, the current in finely divided carbon suspensions[80,81] arises from the reduction of quinoid groups transferred to the solution from the surface of the carbon particles. In transparent colloidal solutions of iron hydroxide (particle radius < 0.1 μm) a reduction wave is observed[82] rather than a maximum. Evidently, the reduction of these colloidal solutions is governed by the same diffusion laws as the reduction of ions in true solutions.

Pairs of maxima have been observed in the reduction polarograms of mixtures (HgS and PbS[53], HgS and FeS[54]). However, the appearance of two current maxima does not necessarily imply that the potential of maximum attachment is different for the two kinds of particle. The particles of the two compounds adhere to the electrode over a wide range of potential, which includes the zero-charge potential, but only the mercury sulphide particles can be reduced at low negative potentials. At the same time, the film of mercury sulphide[61,62] formed on the electrode because of the presence of sulphide ions in the suspension is also reduced. At more negative potentials the reduction of the PbS and FeS particles can take place—or catalytic hydrogen evolution in the presence of FeS—and the second maximum is formed, followed by a decrease in current due to the loss of adhesion at sufficiently negative potentials.

A pair of maxima is observed also in the reduction polarograms of suspensions of manganese dioxide, plotted with a dropping mercury electrode in solutions of sulphuric acid and ammonium sulphate: the first maximum occurs at +0.1–(–0.2) V s.c.e., the second at much more negative potentials [–(1.3–1.4) V][65]. Their origin is not discussed[65], but it is assumed that solid particles are reduced in both cases (to give manganese ions of different valencies). However, the first maximum is more likely to be due to the reduction of mercury ions, formed by the direct oxidation of the metallic mercury of the electrode by particles of adhering manganese dioxide. (A weak electrocapillary attachment can be expected even at the potentials of the first maximum, since they are not too far removed from $\varphi_{\epsilon=0}$.) We have shown[83] that mercury ions can be formed in the presence of an oxidising agent. The fall in current after the first peak can be ascribed to the inhibiting effect of the increasingly cathodic potential on the reaction between the manganese dioxide and the mercury. Reduction of MnO_2 occurs at high negative potentials (second peak). Although the electrocapillary attachment is not very strong at these potentials, the particles colliding with the electrode can overcome the disjoining effect of the interfacial layer of electrolyte and remain briefly in contact with the electrode. The reduction process is accompanied by catalytic hydrogen evolution[65], made possible by the decreased overvoltage on the MnO_2 particles.

A second maximum at very cathodic potentials(–1.2 V relative to the normal calomel electrode) has been observed also in the reduction polarograms of heat-treated silver carbonate[84]. This maximum is ascribed to the formation of a new form of silver carbonate with a high density of lattice defects; it is not very sharply defined, and consists of a collection of current surges probably associated with particularly energetic collisions outside the region of electrocapillary attachment.

Thus we may conclude that particles of a suspension of insoluble material are reduced at a dropping mercury electrode by virtue of the electrocapillary attachment of the particles to the electrode in the region of potentials around $\varphi_{\epsilon=0}$, or by collisions between the particles and the electrode at potentials not too far removed from this value. The following conditions are necessary: 1) the reduction potential of the insoluble substance must not be more negative than the region of potentials at which attachment occurs: 2) the particle size of the suspension must be greater than average colloidal dimensions ($r > 1$ μm), i.e. the suspensions must be coarsely disperse according to the conventional classification used in colloidal chemistry: 3) stirring (not necessarily vigorous) of the suspension is essential.

In all the work discussed above stirring was produced by a stream of inert gas or by a magnetic stirrer. However, the random collisions of the particles with the electrode produce irregular current surges, and therefore the polarograms are not easy to reproduce. A novel design of polarographic cell has been proposed[85] with the aim of providing a more regular stream of particles colliding with the electrode: a stream of gas, supplied at a constant flow rate, induces circulation of the solution towards the electrode, also at a constant rate. External means of ensuring regular drop detachment are provided. A cell of this design was used to measure the rate of dissolution of lead salts in various media, but the results were disappointing[85]. Evidently, an even flow of particles towards the electrode had not been achieved.

VII. BEHAVIOUR OF SUSPENSIONS ON AN AMALGAMATED ROTATING-DISK ELECTRODE

An even flow of the particles of a suspension towards the electrode can be achieved only by using a rotating disk electrode. Suspensions of activated oxidised carbon[86,87] and of insoluble mercury halides[88] have been studied on an amalgamated rotating-disk electrode. Strong attachment of the particles to the electrodes is again observed in the potential region corresponding to the point of zero charge of mercury. However, the region of electrocapillary attachment is much broader with the rotating disk electrode than with the dropping mercury electrode, and can extend over 1.0–1.1 V. This is because the layers of electrolyte between the solid particles and the electrode surface are more easily disrupted when the electrode is a rotating disk, which produces a very energetic flow of particles, and adhesion becomes possible at potentials quite far removed from $\varphi_{\epsilon=0}$. Carbon particles attached to the electrode[86] are retained even when the potential is moved still further from $\varphi_{\epsilon=0}$: down to potentials of –(1.7–1.9) V s.c.e. At still more cathodic potentials the particles are eventually detached. Thus, with carbon suspensions the amalgamated electrode is covered with particles over a range of potentials extending over almost 2 volts.

In the polarisation curves given by suspensions of oxidised carbons the reduction current is directly proportional to potential over a wide range of potentials. This current is due to the reduction of oxygen groups on the surface of carbon particles attached to the electrode (Fig. 6). The steeper increase in current which sets in at –(1.0–1.2) V in neutral and in alkaline solutions, and at –(0.7–0.8) V in acid solutions, is due to the evolution of hydrogen on the surface of the particles, since the hydrogen overvoltage on carbon is lower than on mercury. The polarograms for the neutral and the alkaline electrolyte show a steep fall in current at –(1.7–1.9) V, due to the detachment of the carbon particles. In acid solutions the detachment potential is not reached because hydrogen evolution begins at lower voltages. (Note that detachment is not observed

with the dropping mercury electrode, discussed in Section VI, because the surface of that electrode is constantly renewed.) The detachment is the result of the enhanced disjoining action of the interfacial layer of electrolyte at potentials sufficiently far removed from $\varphi_{\epsilon=0}$. The reduction currents of attached particles are independent of the rate of rotation of the electrode, but they show a slight increase with the "concentration" of the suspension. The detachment potential of the particles, on the other hand, depends on the rate of rotation of the electrode (ω): the greater ω, the more readily are the particles detached, evidently because of the centrifugal forces acting on them[86].

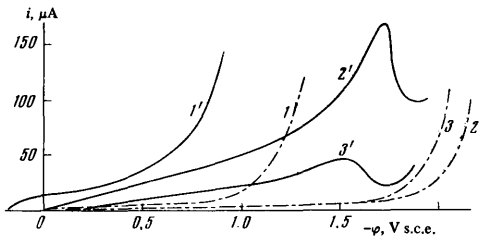


Figure 6. Polarisation curves measured with an amalgamated rotating-disk electrode in 0.1 M solutions of $HClO_4$ (*1*, *1'*), KCl (*2*, *2'*), and KOH (*3*, *3'*) in an argon atmosphere without (*1*, *2*, *3*) and with (*1'*, *2'*, *3'*) a suspension of positive oxidised carbon; ω = 3890 revolutions min^{-1} (from Ref. 86).

In the course of studies of carbon suspensions it was realised that information could be obtained on a number of electrochemical processes (such as the reduction of dissolved molecular oxygen and hydrogen peroxide[86,87]) which can occur on the surface of carbon particles attached to the electrode. By making a number of simplifying assumptions, the degree of screening (θ) of the surface of the amalgamated electrode by the carbon particles could be calculated[86]: it was found to be independent of the rate of rotation of the electrode, but slightly dependent on pH (θ = 0.4 in alkaline electrolyte and 0.5 in a neutral electrolyte). In acid solutions θ cannot be evaluated, but it is reasonable to assume an even higher screening because the reduction currents in acids are higher than in alkalies by a factor of 2–4.

The reduction currents on a rotating amalgamated electrode of suspensions of mercury halides are an order of magnitude greater than the reduction currents of carbon suspensions on the same electrode, since the whole of the attached particle is reduced, and not just the oxidised surface groups[88]:

$$Hg_2Br_2 + 2e \rightarrow 2Hg + 2Br^- \qquad (12)$$

Thus, under reducing conditions the particles of mercury halide attached to a rotating amalgamated electrode are continually disappearing, and the electrode surface is continually restored: this is shown in the polarograms by periodic negative current surges. Hence, the steep fall in the polarographic current (Fig. 7) is not due to the detachment of particles, but to the weakening of the electrocapillary attraction effect as the potential swings beyond $\varphi_{\epsilon=0}$. Increasing the speed of rotation of the electrode strengthens the onrush of the particles towards the surface, and helps them to overcome the disjoining effect of the interfacial layers of electrolyte at more negative potentials, thus causing a shift of the sharp drop in current towards more negative potentials.

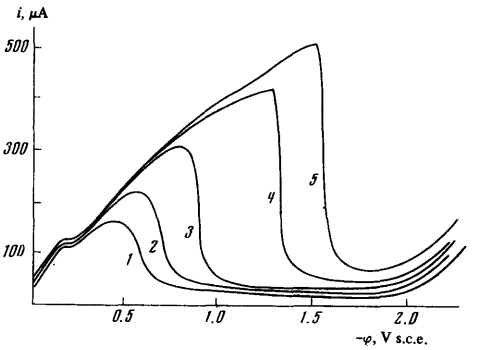


Figure 7. Polarisation curves for the reduction of a suspension of Hg_2Br_2 (0.05 mole $litre^{-1}$) in 0.1 M Na_2SO_4 on an amalgamated rotating-disk electrode: 1) ω = 1030, 2) 1970, 3) 3890, 4) 5700, 5) 7660 revolutions min^{-1} (from Ref. 88). Periodic current surges are not shown.

The fact that the suspensions do not give a reduction current at high negative potentials, in spite of the very vigorous stirring and of the powerful collisions of the particles with the surface of the disk electrode, is further proof of the reality of the attachment of particles to the surface of a mercury or amalgamated electrode at potentials close to $\varphi_{\epsilon=0}$, and strengthens our conclusion that direct reduction of the solid particles of a suspension under polarographic conditions can occur, in general, only if the particles are attached to the surface of the electrode.

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Our recent study of mercury halide suspensions on a solid (rotating) disk electrode[89] has shown that the particles of coarse suspensions do not adhere to the surface of a solid electrode. Accordingly, no reduction currents are produced by the particles of these suspensions. Most probably, the electrocapillary attachment of solid particles to an electrode surface is possible only when the surface is liquid (as in the case of the dropping mercury electrode or the amalgamated electrode), i.e. mobile and capable of sufficient deformation to produce the angle of contact at the three-phase boundary (electrode–electrolyte–particle) needed to accommodate the capillarity forces which hold the particle to the electrode surface. Frumkin[77] has invoked deformation of the surface of a liquid electrode in his discussion of the attachment of gas bubbles and of glass surfaces to mercury. It should be noted that small, colloidal particles were always present in the coarse suspensions of mercury halides used in our work with a rotating electrode. These particles are reduced at a platinum electrode (see Section IV): they can reach the electrode surface by diffusion, and furthermore these very small particles are subject to forces of adhesion (but not electrocapillary attraction) to the electrode by virtue of their roughness and of their surface charge.

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Kirov State University of Kazakhstan,
Alma-Ata

U. D. C. 543.544.42

Quantitative Cusp Paper Chromatography

V.N.Aleskovskaya and V.B.Aleskovskii

A relative assessment of the main methods of quantitative chromatography is given. The theory and practice of cusp chromatography (a new variant of precipitation chromatography, developed by the writers) are discussed, and examples are given of the determination of cations and anions, singly and in mixtures, and over a very wide range of concentrations. 38 references.

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I. INTRODUCTION

A short review of the development of precipitation chromatography, beginning with the work of its originators (Gapona and Gapon[1,2]), and also a discussion of the theory and many interesting practical applications of precipitation chromatographic analysis, can be found in the monograph by Obshanova and coworkers[3], and more recent developments in a review article by Lur'e[4]. The potential uses of partition chromatography are discussed in a recently published symposium[5].

The bands of precipitation chromatograms are formed by chemical reactions under well defined and reproducible conditions. The direct proportionality between the size of the bands in precipitation chromatograms and the amount of material being analysed has been stressed by many workers[7-14]. This feature of precipitation chromatography distinguishes it from partition and from sorption chromatography, and offers (in principle) a simple and reliable method of quantitative determination by measuring the size of the bands in precipitation chromatography. The most convenient form of the method from this point of view is precipitation chromatography on paper, and in particular one of its variants which allows the bands to be obtained in the shape of cusps[15]. However, much of the earlier work was aimed at the study of chromatograms of a different type[7,16-18]. No attempt was made to determine the optimum conditions for the formation of cusp chromatograms, and even the reason for the formation of bands in the shape of cusps was not discussed. In general, cusp chromatography was ignored. A recent symposium[5] deals with quantitative chromatography by physicochemical methods: in the present review we shall discuss the direct determination of the amount of material in the band by measurements of the size of the bands (and, in particular, the height of the cusps[6]).

II. QUANTITATIVE CHROMATOGRAPHY BY MEASUREMENT OF THE SIZE OF BANDS

There is general agreement[4] that sorption and partition chromatography on columns do not lend themselves to quantitative determinations from measurements of the size of the bands, mainly because these bands have indeterminate stoichiometries and geometries. The concentration of the substance being analysed in the bands, and the size and shape of the bands themselves, show a complicated dependence on the composition and concentration of the solution under study, on the composition and specific surface area of the sorbent or of the carrier—stationary phase mixture, and also on the dynamics of the process (which can be further complicated by diffusion in the bulk of the sorbent or through the porous carrier). On the other hand, paper chromatography and thin-layer chromatography offer the possibility of quantitative analysis directly from the chromatogram (e.g. by scanning the bands with a densitometer or with a radioactivity detector if suitable tracers are used). However, we cannot yet "rely on the reproducibility and precision of the results"[5]. This is not surprising, since the composition of the stoichiometrically indeterminate bands depends on the chromatographic conditions and on the relative order and duration of the various steps. These uncertainties disappear completely when we turn to precipitation chromatography on paper: bands consisting of precipitates have a definite stoichiometry and (in the case of paper chromatography) a very small and constant thickness. Simple calibration (by determining the width of a standard band) is sufficient for precise measurement of the amount of material present in the precipitate: this presupposes that the sample for chromatography is deposited on the paper as a band of constant width, or (preferably) that the band is produced in the form of a cusp with a constant, narrow base[15].

Kokk and Aleskovskii[19,20] were led by similar considerations to use thin threads as columns of the wick type, and were able to claim enhanced sensitivity for quantitative column chromatography.

The paper specially produced for chromatography has a constant density. If a uniform, stationary layer of precipitant is deposited on such a paper, quantitative chromatography of substances which form sparingly soluble compounds with the precipitant becomes possible.

An immobile layer of precipitant—one of the main requirements of quantitative chromatography—is obtained by impregnating the paper with a relatively insoluble precipitant. Soluble precipitants should be avoided, because they are partially eluted during the chromatographic separation and the reproducibility of the results is thereby impaired. For this reason, the more recent work[22-24] on cusp paper chromatography was done with paper impregnated with sparingly soluble precipitants, in contrast to the earlier work[15,20,21], in which the cusps had been obtained on paper impregnated with soluble reagents. This small improvement has resulted in satisfactory

reproducibility of the cusps and has established cusp chromatography as a strictly quantitative method.

A uniform distribution of precipitant in the bulk of the paper is obtained using appropriate impregnation conditions, established experimentally. The uniformity of the precipitate in a column of inert carrier has been demonstrated[25,26] by scanning the column (anhydrous alumina) with a counter after precipitation of silver iodide containing radioactive iodine. The uniformity and the attachment of the precipitate on paper are, obviously, no worse than in a column, as shown by the excellent reproducibility of quantitative measurements on paper impregnated with sparingly soluble precipitants. The layer of deposit is believed[25] to consist of charged colloidal particles which are held on the surface of the carrier by electrostatic attraction. Recrystallisation, leading to growth of the primary crystals, is also thought of occur.

The exact size of the band is ultimately determined by the particle size of the precipitate. Hence it is important to adopt chromatographic conditions favouring the formation of crystallites of a reproducible size.

In order to ensure that the whole of the sample deposited on the chromatographic paper comes into contact with the impregnant (precipitant), the primary chromatogram is eluted in various ways[3] with a solution free from the ions being analysed. For example, the paper containing the sample can be steeped in water or in an aqueous solution of glycerol to elute the primary chromatogram.

Another important condition for good results in quantitative paper chromatography is a large difference in solubility between the impregnant and the precipitates of the elements being analysed. Evidently, the impregnant should be more soluble than the precipitates. Under these conditions, Lur'e concludes[4] from a consideration of the dynamics of sorption that "we can expect a discrete distribution of the precipitates in eluted chromatograms in the form of individual bands, practically free from impurities of other components", as other workers had previously reported from experimental work.

The solubility of the precipitates in the various bands can be increased by varying the acidity of the chromatographic solution or by increasing the concentration of complexing agents in solution. It follows that the pH must be optimised and controlled, and in general the concentration of all the constituents of the solution which influence the solubility of the precipitates in the chromatographic bands must also be controlled.

Yet another important condition to be satisfied in quantitative chromatography is very rapid formation of the precipitates: this must be faster than the rate of penetration of the solution through the paper during elution[27].

The difference in the degree of utilisation of the precipitant observed during chromatographic separation of different ions, e.g. zinc sulphide during the separation of silver and copper ions, is ascribed to the different rates of the corresponding replacement reactions: "this difference is greatest when the difference in solubility product between the reactants and the final products is greatest[28]".

Kulaev points out[16,29] that the size of the bands of various precipitates varies in direct proportion with the following factors: 1) the solubility product of the sparingly soluble precipitate; 2) the concentration of the original solution; 3) the drop volume of the original solution. It is also "determined by the conditions under which the precipitate is formed, particularly since the last stages of formation of the precipitate take place in the narrower regions". Kulaev also stresses that "other conditions being the same, the width of the band ... depends only on the solubility product of the sparingly soluble compound", a fact which he ascribes to the dependence of the rate of migration of the precipitation front upon the solubility product. Lur'e[4] does not accept this argument, and suggests that the width of the band is determined by the difference in reaction rates of the components of the solution with the precipitants, which is directly related to the difference between the solubility products of the impregnant and of the precipitate in the final chromatographic band.

Obviously, this controversy can be resolved by a study in depth of the mechanism of precipitation chromatography.

True precipitation chromatograms on paper are often obtained in simple spot tests[30,31]. For example, 0.05—0.25 μg of copper can be detected on paper impregnated with rubeanic acid in the presence of a large excess of cobalt and nickel. These elements produce separate, differently coloured annular bands on the paper. According to Feigl[31], unsized paper is simply an assembly of compressed fibres. The mixture to be analysed is separated by diffusion and adsorption in the capillaries of the paper. The precipitate formed in the interstices between the paper fibres has a fine-grained structure: it can migrate with the solution, cover the surface of the fibres, and eventually plug up the capillaries. In this way a small amount of precipitate can cover a relatively large area of paper, thus making the spot test on paper more sensitive than on a smooth tile or in a test-tube. Because of their small particle size and large surface area, the precipitates formed in the capillaries of the paper are more soluble than the same precipitates formed in test-tubes.

The sensitivity of spot tests can be increased by treating the paper with gelatine. The main difference between paper chromatography and spot-test analysis resides in the method of applying the sample and in the subsequent treatment of the chromatogram. Kulaev[16-18,29] suggests the following procedure[16].

Filter-paper is impregnated with 1—4% solutions of sodium silicate, hydrogen phosphate, or arsenate, or with solutions of potassium ferrocyanide or chromate. The excess of solution is allowed to drain off, and the paper is air-dried whilst still hanging in a vertical position. Samples of the solutions to be analysed are deposited from a capillary dropping pipette or a microburette (drop volume 0.025 ml) on a 65 mm square piece of the paper. The drop should be allowed to fall on the paper from a height "no more than 5 mm from the surface". A circular spot is formed on the paper. This primary chromatogram is eluted by adding 5—6 drops of water, each drop being allowed to spread fully before the next drop is added. The colourless bands are developed by spraying a suitable developer, in repeated small doses, onto the dried chromatogram.

When a mixture of two or more elements is chromatographed, the band corresponding to the least soluble of the elements remains in the centre as a circular spot; the more soluble precipitates surround the central spot in concentric rings disposed in order of increasing solubility. In Kulaev's experiments the impregnated paper contained a small excess (a factor of 2—3) of precipitant over the amount required to react with the ions under study (mercury, iron, bismuth, chromium, aluminium, cadmium, lead, silver, copper, zinc, manganese, cobalt, nickel, barium, strontium, and several others). The width of the band was measured to the nearest 0.1 mm. The procedure used in cusp chromatography, though outwardly similar, is fundamentally different.

This method of quantitative chromatography was first proposed[15] for the determination of copper and nickel on paper impregnated with a 0.1% aqueous solution of sodium diethyldithiocarbamate or a 0.1% alcoholic solution of rubeanic acid (for copper) or with a 1% alcoholic solution of dimethylglyoxime or rubeanic acid (for nickel). A drop of a solution of copper or nickel salt of known concentration is deposited from a calibrated capillary pipette (1.5 μl volume) on a piece of paper impregnated with the appropriate reagent. The edge of the paper below the drop is immersed in a 14% aqueous solution of glycerol contained in a beaker covered with a glass plate. The solvent is drawn into the paper: it entrains any ions which have not yet reacted, and transports them upwards, forming a cusp-shaped band.

The height of the cusp was found to be linearly related to the concentration of the ion being determined and to the amount of precipitant on the paper. By analogy with the spot-test technique, an attempt was made to increase the sensitivity of the determination by treating the paper with a 0.013—0.05% solution of gelatin after the deposition of the precipitant. This amount of gelatin has a negligible effect on the speed of travel of the solvent, but it gives a sharper and more deeply coloured spot.

Kokk and Aleskovskii[21] subsequently developed a method of determining as little as 5×10^{-2}% of copper in micro-quantities of cadmium selenide (0.50—1.00 mg) on grade B chromatographic paper (density 85 g m^{-2}) impregnated with sodium diethyldithiocarbamate. The relative error of the determination was not greater than 17%; cadmium ions interfere, and they had to be removed from the cadmium selenide.

The same authors[19] determined submicrogram amounts of copper in micro-quantities of cadmium selenide (0.5—1.0 mg) on cotton, artificial silk, and natural silk fibres.

Analysis on fibres is probably the most attractive variant of the quantitative chromatography of elements. Whereas in paper chromatography only the thickness of the bands is constant, it is possible to standardise both the thickness and the width of the bands by using fibres of constant diameter, and furthermore the sensitivity of the method can be increased dramatically by choosing very narrow fibres and by measuring the length of the bands under a microscope. Thus, amounts of copper as small as 5×10^{-4} μg were determined in the above experiments[19]. However, paper chromatography is simpler and more convenient for visual estimation, and therefore cusp chromatography is more likely to find general application.

III. THE CUSP PAPER CHROMATOGRAPHY METHOD

The potential advantages of cusp chromatography as a method of chemical analysis and physicochemical research have been demonstrated in the writers' laboratory[22-24,27,32-34].

1. Chromatographic Procedure

In the preferred method[23,27,32], sheets of chromatographic paper (density 90 g m^{-2}) are cut into 6×15 cm strips. Each strip is drawn through a solution of impregnant of the required concentration. In order to produce a precipitate on the fibres of the paper, the sheet is also drawn through a solution containing a 1.5—2-fold excess of precipitant (as compared to the concentration of the ion to be analysed in the test solution).

The impregnated paper is dried; for work at maximum sensitivity the paper is impregnated with a solution of gelatin and dried again.

Paper containing a stoichiometric amount of precipitant ion is prepared by introducing the precipitant ion first, followed by the exchangeable ion (grade "O" paper). The paper can also be impregnated in the reverse order: the exchangeable ion first, followed by the precipitant ion, i.e. the ion of opposite sign to the ion under test. Due to sorption effects, this procedure gives a paper containing an excess of the precipitant ion (grade "R" paper).

Two pencil lines are drawn on the impregnated paper: an immersion line (0.5 cm from the edge of the paper) and a start line (2—2.5 cm from the edge of the paper). Four or five pencil marks are made on the start line 1.0—1.5 cm apart. Solutions of the test ions are deposited on these marks by touching the paper with calibrated glass pipettes of 0.001—0.002 ml capacity, drawn out to a conical point and ground to a smooth tip.

The paper strips with their spots of test solution are dried in the air: the resulting primary chromatograms are eluted in a 500 ml beaker containing 50 ml of a 12% aqueous solution of glycerol, or water, into which the paper is dipped up to the immersion line. The chromatogram is held in the beaker by means of a glass plate and Petri dish of special design, which ensures that the paper cannot touch the bottom or the walls of the beaker. As the solvent seeps into the paper, it entrains the ions under test which have not yet reacted and displaces them upwards. At the end of the experiment, the precipitate (which does not move with the solvent) forms a trace in the shape of a regular cusp. The elution time is 30—40 min: when elution is complete the chromatogram is air-dried for 10—15 min and the height of the cusp is measured with a pair of dividers and a ruler. The reproducibility of the measurements is good, and in practice only 1 or 2 measurements are needed once the procedure has been established.

In some chromatograms the band fails to develop fully, and only the initial part of the cusp is visible. The apex of the cusp must then be found by extrapolation, by producing the sides of the cusp until they intersect.

2. Conditions Under Which Cusp Chromatograms Are Formed

The chromatographic conditions have been fully discussed by one of us[27].

a. The primary chromatogram

We assume that the paper is uniformly impregnated with a sparingly soluble, microcrystalline precipitant for the ion under test. The volume of the sample of solution, and the thickness and density of the paper, are constant.

As soon as the solution from the capillary pipette begins to wet the paper, precipitate begins to form in a cylindrical region of increasing diameter d (see Fig. 1), and solution denuded of the ions being chromatographed (say, A_a^-) begins to filter outwards through the cylindrical surface of this region.

Some of these ions are transferred to the precipitate by an exchange reaction with the impregnant, and some are adsorbed onto the precipitate. Thus, the ions being chromatographed are held within a cylinder of diameter d, as though it were a chromatographic column, consisting of a very thin layer of freshly deposited $M_u A_a$ spread over

the surface of the paper fibres and therefore in a highly reactive state. As the concentration of the ion under test in the original solution increases, the diameter of this column also increases until it becomes comparable with the diameter of the water spot d_w. Initially, as long as the ions in excess of the stoichiometric requirements of the impregnant are held only by sorption forces, the quantity of both adsorbed and precipitated ions is proportional to the volume of the column, and therefore the total amount a of ions under test is a function of the volume of the column and hence of the square of its diameter. We can write

$$d = D\sqrt{a} \qquad (1)$$

where D is a constant coefficient. However, as d approaches the value d_w, the processes by which the test ion is accommodated in the spot become more complicated.

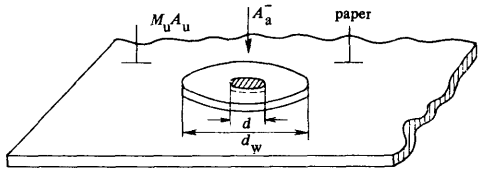


Figure 1. Spot formation in the primary chromatogram.

When the whole of the impregnant within the spot has reacted to give a precipitate (e.g. $M_uA_a.nM_aA_a$, where nM_aA_a denotes the amount of adsorbed ions in excess of stoichiometry), increasing amounts of the free compound (M_aA_a) of the test ion begin to accumulate within the volume of the spot. This effect complicates the relationship between the diameter of the spot and the amount of ions under test. Finally, in the limit the spot size becomes constant, for obvious reasons:

$$d = d_w = \text{const.} \qquad (2)$$

Evidently, within the range of a values to which Eqn. (1) can be applied we can use the spot diameter to characterise the sorption of ions by their precipitates, and thus investigate precipitation reactions quantitatively.

The quantitative study of the sorption of ions by their precipitates in the form of primary bands in paper precipitation chromatograms has been discussed[27] by reference to the following observations. With very small samples of ions, just above the limit of detection, the spot diameter of the primary chromatogram is always smaller than the diameter of a water spot deposited on the paper with the same capillary pipette.

Thus, in experiments with a 2 μl pipette the diameter of the water spot was 0.70 cm. The diameter of a spot of silver iodide (containing 0.5 μg of iodine) was only 0.50 cm, and copper diethyldithiocarbamate gave spot diameters of 0.55 and 0.10 cm for copper contents of 0.5 μg and 0.01 μg respectively. As the content of the chromatographic ion in the sample is gradually increased, the spot diameter in the primary chromatogram increases almost exactly as expected on the assumption that the ion is adsorbed on its precipitate. The departure from a straight-line relationship at small values of a can be ascribed to sorption of the test ion on the precipitate formed by a double decomposition reaction between the test solution and the impregnant, and not to sorption of the test ion on the paper[27].

b. The secondary chromatogram, and cusp formation

As stated above, the secondary chromatogram is obtained by eluting the primary chromatogram with a solvent (e.g. aqueous glycerol, or pure water). Elution is carried out simply by allowing the solvent to seep into the paper. The spot containing a precipitate, formed in the primary chromatogram, may or may not retain an excess of the precipitant. Hence we can define two special cases[32]:

$$\text{I. } a \leqslant uS; \quad \text{II. } a > uS$$

where u is the titre of the paper (mg-equiv cm^{-2}), and S is the area of the spot of precipitate (cm^2).

In the first case the whole of the sample of ions within the spot is bound in the precipitate as M_uA_a or M_aA_u, but in the second case only part of the test ions is bound (by precipitation or sorption on the precipitate), and the remainder is in its original form of the soluble compound M_aA_a and its ions. In this latter case the stoichiometric excess of ions will be washed out of the circular spot by the eluting solvent and carried along the interstices of the paper, where it will meet a fresh supply of the impregnant M_uA_u. Under these conditions, the precipitation of the ion under test will extend beyond the area defined by the primary spot.

The inequality $a \leqslant uS$ defines the system studied by Kulaev[16-18,29] and others, whereas the inequality $a > uS$ defines the conditions for cusp chromatography. In the first case the size of the bands on the chromatograms is determined mainly by the solubility of the precipitates and by diffusion of ions, and is related to the concentration of the ions only through the diffusion effect. In the second case ionic diffusion plays only a secondary role: the main contribution comes from convection, i.e. the transport of ions by the flow of solution.

Depending on the magnitude of the difference

$$a - uS = \Delta \text{ mg-equiv.}, \qquad (3)$$

a more or less extensive trace of the ion under test is formed on the paper in the direction of motion of the solvent, and under favourable conditions this trace has a regular cusp shape.

A simple geometrical construction is sufficient to show that cusp formation must follow from the circular shape of the original spot and from the uniform transport of ions under test along the plane of the paper by the flow of eluent (Fig. 2). The quantity of ions transported by the solvent from different section of the circular spot decreases from the centre towards the periphery, in inverse proportion to the length of the chord parallel to the direction of flow. It has been shown experimentally[27] that regular cusps can be obtained by allowing solvent to seep into the primary chromatogram only if the original spot is truly circular, and then only if the moving solvent front remains strictly parallel to the edge of the paper immersed in the liquid.

3. Fundamental Aspects of Cusp Chromatography

As stated above, the height of the cusp increases with the difference $\Delta = a - uS$. Obviously, it must decrease as the titre of the paper (u) increases. This relationship can be expressed by the formula

$$h = \frac{k_1\Delta}{u} = \frac{k_1(a - uS)}{u} \quad (4)$$

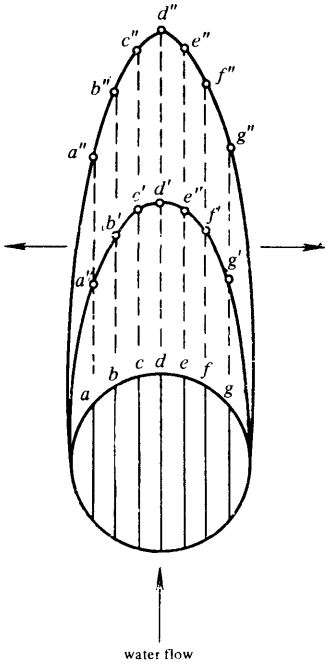


Figure 2. Cusp formation. The points a, b, c, d, e, f, g correspond to the condition $a \leqslant uS$; the points marked with the single prime and the double prime correspond to a small excess and a large excess, respectively, of the test ion in comparison with uS.

This equation was deduced[27] by assuming that the cusp can be approximated by a triangle of height h connected by its base to a semicircle of diameter a (equal to the diameter of the circular spot in the primary chromatogram).

The titre of the paper is approximately equal to the ratio of a to the height of this triangle:

$$u \simeq \frac{2a}{dh} \text{ mg-equiv. cm}^{-2} \quad (5)$$

If the sample volume and the titre of the paper remain constant, the product uS is constant to a first approximation, and the height of the cusp is linearly related to the quantity of ions in the sample:

$$h = \frac{k_1 a}{u} - k_1 S = k_2 a - B \quad (6)$$

Hence

$$a = \frac{h + B}{k_2} \quad (7)$$

As an example of the application of this linear relation, we may quote the results obtained for the chromatographic analysis of iodide ions on paper impregnated with silver chloride[22-24], and also of silver ions on "O" grade paper impregnated with lead diethyldithiocarbamate[27,32]. From the same data, plotted as $h = f(u)$ for constant a, we obtain a family of hyperbolae.

It is possible to calculate[27] the concentration P of the precipitant in solution which should be used to impregnate the paper for the chromatographic analysis of a mg-equiv of an ion. The calculation assumes that the strip of paper retains V ml of the solution of impregnant, and that the whole of the precipitant (G grams) contained in this volume remains in the paper after impregnation. For dilute solutions we can write

$$\frac{G \cdot 100}{V} = P, \%,$$

whence

$$G = \frac{P \cdot V}{100}$$

and the titre of the paper is $u = \dfrac{G.10^3}{\text{equiv wt.} S_p}$ mg-equiv cm^{-2}, where S_p is the area of the strip of paper in cm^2. Inserting the value of G into this formula we obtain

$$u = \frac{PV \cdot 10^3}{\text{equiv. wt.} \cdot S_p \cdot 100} = \frac{10PV}{\text{equiv. wt.} \cdot S_p} \quad (8)$$

Then, using formula (5), we obtain an expression relating the percentage concentration of the solution of impregnant to the amount of ions under test and to the cusp height:

$$u \approx \frac{2a}{dh} \simeq \frac{10PV}{\text{equiv. wt.} \cdot S_p}, \text{ whence}$$

$$P = \frac{2a \text{ equiv. wt.} \cdot S_p}{10 \cdot Vdh} = \frac{0.2 \text{ equiv. wt.} \cdot S_p}{Vdh} \quad (9)$$

All the quantities in formula (9) are either known or easily determined experimentally.

Formulae (5) and (8) have been tested[27,35] by direct analytical determinations of the titre of the paper.

Having established the titre of the paper, known amounts of iodide, bromide, and thiocyanate were chromatographed. The results were used to calculate the titre of the paper by formula (5), and an independent estimate of the titre was obtained by inserting the volume V of impregnant solution and the area S_p of the paper into formula (8).

The titre of the paper calculated by formula (8) agrees with the results of chemical analysis within experimental error, and the values obtained by the approximate formula (5) are also in fairly good agreement.

For thiocyanate these values are closer to the titres obtained by direct chemical analysis than for iodide and bromide. This is because, as shown by chemical analysis of the precipitates in the halide cusps, the atomic ratio of iodide and of bromide to silver increases and tends to 1.5 as the titre of the paper and the amount of halide are increased, suggesting the formation of a complex of the type $K_2Ag_2I_3$. For thiocyanate, on the contrary, the ratio decreases from 1.0 to 0.7. Thus, the effective equivalent of the halide was not the same as the assumed value. Hence we conclude that formula (5) should include a correction equal to the atomic ratio of the amount of precipitant ion (for example, M_u^+) to the amount of the chromatographic ion:

$$u \approx \frac{2a}{dh}\left(\frac{M_u^+}{A_a^-}\right) \approx \frac{2a}{dh} \cdot n \quad (5a)$$

The values given by formula (5a) for the titre of the paper agree somewhat better with the results of chemical analysis.

It is worth noting that, if the titre of the paper is known, the composition of the precipitate in the cusp can be determined from chromatographic data only (d, h, and a): this is a very rapid method of determining the composition of complexes in the solid state.

4. Sensitivity Considerations

The smallest amount of an element which can be estimated by chromatography is that which corresponds to the smallest reproducible cusp height h_0: we find[27] that $h_0 = d$, where d is the diameter of the primary circular spot. Hence, the sensitivity of determinations by the cusp method is approximately the same as that of the corresponding spot tests. In general, the reproducibility of analytical procedures becomes acceptable when the sample size is at least one order of magnitude greater than the limit of detection: we therefore recommend[27] a choice of conditions leading to a minimum cusp height of 10 spot diameters.

The sensitivity of the cusp method is influenced by a number of factors, the most important being those which determine the solubility of the precipitate in the cusp. They include: the pH of the solution, the concentration of complexing agents in solution, the ionic strength and temperature of the solution, the volume of the eluting solution held by the paper, and some others.

Obviously, we should consider first of all the volume of solution taken up by the paper, which directly determines the amount of impregnant which dissolves and hence the amount of precipitate formed by the ion under test.

When the solution used to elute a primary precipitation chromatogram rises to a height H in a strip of paper of width L, the compound of the test ion M_uA_a (e.g. AgI) can form a cusp only if it is present in sufficient amount to saturate a volume $V = H.L.\delta$ cm^3 (where δ is the thickness of the paper) without going completely into solution.

If 1 ml of a saturated solution of M_uA_a contains a_p mg-equiv of the test ion, the paper strip will contain $V.a_p$ mg-equiv of the ion in solution. Hence, if the sample contains a mg-equiv of the test ion, the amount which goes into the precipitate is

$$a - V \cdot a_p = a^* \text{ mg-equiv.} \qquad (10)$$

The height of the cusp is correspondingly decreased, i.e. the dissolution of the precipitate lowers the sensitivity of the determination. Let a^* equal u_0S (the smallest quantity of precipitate of the test ion which can be detected on paper). Inserting this quantity into Eqn. (10) we obtain $a - V.a_p = u_0S$. Hence we arrive at an expression for a_0, the sensitivity of the chromatographic analysis:

$$a_0 = Va_p + u_0S \qquad (11)$$

In the simplest cases, for example in the determination of halide and thiocyanate ions on paper impregnated with silver chloride, we can assume

$$a_p = [A_a^-] \text{ g-ion litre}^{-1}$$

From the equation for the reaction $M_uA_a \rightleftharpoons M_u^+ + A_a^-$ we can write

$$[A_a^-] = \frac{SP_{an}}{[M_u^+]},$$

but $[M_u^+]$ is the solubility of the impregnant, which in the present case can be written $[M_u^+] \simeq \sqrt{SP_{imp}}$. Thus, $[A_a^-] = \dfrac{SP_{an}}{\sqrt{SP_{imp}}}$. Inserting the resulting value of $a_p = [A_a^-]$ into Eqn. (11) gives $a_0 = \dfrac{V.SP_{an}}{\sqrt{SP_{imp}}} + u_0S$. Turning to Eqn. (10), we note that for $a = V.a_p$ the quantity a^* equals 0, i.e. analysis becomes impossible when

$$a = \frac{V \cdot SP_{an}}{\sqrt{SP_{imp}}}$$

or, in general,

$$a_{lim} = \frac{V \cdot SP_{an}}{S_{imp}} \qquad (12)$$

where a_{lim} is the smallest detectable amount of the test ion in the sample, which is a constant for one particular ion and impregnant under a given set of conditions, and S_{imp} is the solubility of the impregnant.

Thus, the sensitivity of the method is higher, other conditions being equal, the smaller the solubility product of the analytical precipitate and the higher the solubility of the impregnant.

One of us[27] has tabulated the values of a_{lim} calculated by Eqn. (12) for thiocyanate, bromide, and iodide on paper impregnated with silver chloride or silver oxide.

It is evident from Eqn. (11) that the sensitivity of detection of ions is determined by their limiting amount a_{lim}, with an additive correction given by the product u_0S. (The latter is greater than a_{lim} by many orders of magnitude for very insoluble compounds of the ion being analysed, but for relatively soluble compounds it does not differ from a_{lim} very significantly.) Hence it is clear that the sensitivity of detection of thiocyanate, bromide, and iodide must increase in the order of decreasing a_{lim}, with very similar values for thiocyanate and bromide. According to our results[27], the sensitivity should be higher on paper impregnated with Ag_2O than on paper impregnated with AgCl. Since the solubility of Ag_2O is greater than that of AgCl†, this conclusion is consistent with the theoretical prediction that the sensitivity must increase with the solubility of the impregnant if other conditions remain constant. Experimental confirmation has been obtained[22-24] that the sensitivity of detection of thiocyanate and halide ions is higher on paper impregnated with Ag_2O than on paper containing silver chloride.

5. Range of Detection of Ions

It can be seen from Eqn. (4) that the height of the cusp can be controlled within any prescribed limits by varying the titre u of the paper. Hence, we can assign to every range of a values a value of u such that the cusp height h will fall within the prescribed limits, e.g. such that the largest cusp shall fill a strip of chromatographic paper 15 cm long. It may be convenient to divide[27] the very wide range of analytical levels of detection found in practice into a number of more limited ranges, each corresponding to a factor-of-ten variation in the size of the sample (e.g. from 10^{-6}—10^{-5} mg-equiv for range 1 to 10^{-3}—10^{-2} mg-equiv for range 4). This allows us to estimate

† The solubilities of AgCl and Ag_2O are 1.2×10^{-5} and 1.9×10^{-4} mg-equiv ml^{-1} respectively.

the amount of ions in each sample under the most favourable conditions, ensuring that the paper is always impregnated with the optimum amount of precipitant.

Clearly, by increasing the titre of the paper we can lower the cusp height by the amount needed to ensure that the cusps for high as well as for low concentrations of the test ion are contained within a chromatogram of a given size. As regards analytical range and sensitivity, the best results are obtained at some particular values of the titre (e.g. 2.0×10^{-5} and 3.3×10^{-5} mg-equiv cm^{-2} for silver and copper respectively).

These general rules for micro-concentrations of test ions can easily be extended to the determination of high concentrations of ions by the cusp method. We have described[27] the chromatographic analysis of concentrated solutions of potassium iodide and bromide up to saturation conditions, with test samples containing up to 500—800 μg of halide.

6. Chromatographic Analysis of Mixtures of Ions

It has been shown experimentally[27] that when the test solution contains a mixture of ions capable of reacting with the impregnant to form a precipitate, a cusp consisting of the least soluble precipitate is formed first of all, followed by the other precipitates in order of increasing solubility.

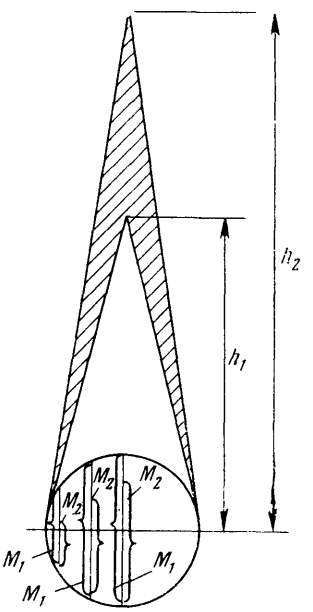


Figure 3. Double cusp formed by two different ions M_1 and M_2 with the same impregnant. (The precipitate formed by M_1 is less soluble than the precipitate formed by M_2.)

Hence, it was suggested that the equality $a_1 + a_2 = uS_1 + uS_2$ (or in general $\Sigma a = u\Sigma S$) can be applied to precipitates of a given type, where a_1 and a_2 are the amounts of two different ions in the sample, u is the titre of the paper, and S_1 and S_2 are the areas of the corresponding bands.

It is evident from Fig. 3 that

$$S_2 \simeq \frac{1}{2} h_2 \cdot d - \frac{1}{2} h_1 \cdot d = \frac{1}{2} d (h_2 - h_1),$$

whence

$$a_2 \simeq \frac{ud}{2} (h_2 - h_1),$$

and putting $\frac{ud}{2} = m$ we obtain

$$a_2 = m (h_2 - h_1) \qquad (13)$$

i.e. the amount of precipitate for the more soluble ion is proportional to the difference in height between the cusps for the more soluble and the less soluble ion.

By a similar argument it can be shown that the amount $a_{(n+1)}$ of an ion mixed with n other ions which form more insoluble precipitates with the same impregnant is proportional to the difference in cusp height

$$a_{n+1} = t \cdot \Delta h \qquad (14)$$

Experiment shows[27] that this relationship applies only when the titre of the paper has been optimised with respect to the ion which forms the most soluble precipitate.

Various mixtures of anions and cations have been analysed by applying these considerations. Thus, mixtures of traces and of relatively large amounts of halides have been chromatographically separated and estimated on paper impregnated with silver oxide.

Precipitation chromatography can be applied in qualitative as well as quantitative analysis. For example, chloride and bromide impurities in potassium iodide can be separated and determined by cutting out the different constituents of the cusp. The effectiveness of this new method of analysis has been confirmed by separating a complex mixture of cations (silver, copper, lead, and cadmium).

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Recent studies[22-24,27,32] of the conditions under which cusp-shaped bands are formed in precipitation paper chromatography have led to the development of a new quantitative method for the determination of ions: cusp paper chromatography. This method differs from existing chromatographic procedures in that it relies on accurate measurements of length, and furthermore it depends on stoichiometric relationships like the classical methods of quantitative analysis. It differs from the latter, however, in being a true chromatographic method, and therefore it offers all the advantages of speed and simplicity which one associates with chromatographic analysis.

Cusp chromatography is a particularly fast method, and is suitable for use in works laboratories and under field conditions, for example in the wet assay of mineral deposits. It can be used to determine anions and cations, in solutions varying in concentration from very dilute to almost saturated. Mixtures of ions as well as single ions can be detected by cusp chromatography, and the method can tolerate the presence of many extraneous substances. 40—50 tests can be done in one hour, and since each test requires only 1—2 μl of solution, a complete analysis can be done on a drop of solution (0.01 ml). The sensitivity of the method is comparable to that of conventional spot tests: for example, 0.2 μg or 1.6×10^{-6} mg-equiv for iodide and 0.02 μg or 6.3×10^{-7} mg-equiv for copper. The relative error of determinations within the same concentration range is 2—10% (for example, 2—7% for iodide ions).

It is important to stress the fact that this is a genuine micro-method of analysis, since only 1—2 μl of solution are needed for each determination. The precision (usually 1.5—11%) can be improved by calibrating the capillary used to deliver the sample (or by using a micro-syringe or micro-pipette), and also by measuring the cusp height to 0.1 mm or better. Evidently, this method of determining micro-quantities of ions can be combined with some method of concentrating trace elements (for example, the "sinking particle" method[36,37]); in this way, the contents of a 1-litre sample of solution can be concentrated into a volume of 0.1 ml, and the range of detection can be extended by 3—4 orders of magnitude.

Another advantage of the method is the possibility of obtaining quantitative information from imperfectly formed cusps, by graphically extending the edges of the cusp and using their intersection to locate the missing apex.

Paper chromatography by the cusp method offers an almost instantaneous method of qualitative and quantitative analysis of large groups of ions (and their mixtures) having closely similar properties: for example, chloride, bromide, and iodide. The elements can be separated by cutting the complex cusp into bands, corresponding to the individual elements.

The theoretical relationships between the height of the cusp and the amount of test ion, and between the height of the cusp and the titre of the paper, and also the formulae for calculating the titre of the paper, have all been confirmed experimentally for both anions and cations. The deviation from linearity of the initial portion of the function $h = f(a)$ has been shown to be due to sorption of the ion by its precipitate (formed by a double decomposition reaction with the impregnant), which is more significant at low concentrations of the test ion. The simple relationship between the diameter of the circular spot formed in the primary chromatogram and the amount of test ion in the sample applied to the paper can be used to study the sorption of various ions by the precipitate formed by their reaction with the impregnant. The observation that a small spot formed within the thickness of the paper acts as a miniature chromatographic column will be applied in future studies of the sorption properties of many precipitates. In the analysis of thiocyanate and halide ions on paper impregnated with silver oxide or silver chloride the cusp height was found to be unmistakably related to the concentration of the silver nitrate solution used to impregnate the paper, and therefore also to the titre of the paper.

However, in the analysis of silver, copper, and some other cations on paper impregnated with metal diethyldithiocarbamates a simple relationship was found only with "O" grade paper, prepared as described above. This observation led to the following empirical rule for the preparation of paper for selective cusp chromatography: the paper should be impregnated first with the precipitant ion, followed by the ion of the same sign as the test ion.

The rule is confirmed by experiments on cadmium and lead, chromatographed singly or in admixture with silver and copper on "R" grade paper, i.e. paper impregnated with lead diethyldithiocarbamate "not according to the rule". Although neither lead nor cadmium should develop a stain on paper impregnated with lead diethyldithiocarbamate, cusps were obtained on this paper, but not on "O" paper (impregnated with lead diethyldithiocarbamate in stoichiometric proportions). This anomaly can be explained only by sorption and coprecipitation phenomena on the "R" grade paper. Evidently, quantitative observations of coprecipitation phenomena can be made on chromatographic paper of this type.

Starting from simple considerations, we have established a relationship between the sensitivity of the determination and the solubility of the precipitates in the simplest case of an exchange reaction between the singly charged test ion and the (more soluble) compound of the singly charged precipitant ion. The resulting formula states that the greater the solubility of the impregnant, and the smaller the solubility of the precipitate formed on the paper by the test ion, the lower is the loss of test ions by dissolution in the eluent and therefore the more quantitative is the formation of the cusp. This explains why the sensitivity increases in the order of decreasing solubility product when a series of ions is analysed on paper of a given titre containing a given impregnant.

Thus, previous assumptions that the size of the bands in precipitation chromatograms is determined by the relationship between the velocity of the precipitate front[16,38] or the rate of precipitation[14,28] on the one hand, and the solubility product on the other hand, cannot be upheld. The same conclusion can be reached, even more simply, by noting that the size of the bands cannot be determined by the rate of any particular process since equilibrium is established when the bands have grown to their full size.

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Elementary Reactions of Oxidation Inhibitors

E.T.Denisov

The review gives a systematic account and a critical analysis of the experimental data on the elementary reactions of phenols and aromatic amines in hydrocarbons undergoing oxidation. The results of the measurements and semiempirical estimates of the strength of the In-H bond (InH = inhibitor) in phenols and aromatic amines are examined. From the experimental data presented in the review, evidence is adduced for reaction mechanisms in the inhibited oxidation of hydrocarbons and a combined approach to the concept of the efficiency of the oxidation inhibitor is formulated.
The bibliography includes 110 references.

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I. INTRODUCTION

Inhibitors of oxidation reactions (antioxidants) have acquired considerable importance in modern chemistry. They are used widely to stabilise plastics, synthetic fibres, rubbers, lubricating oils, fats, and medicinal preparations. Experimental data on antioxidants have been compiled in monographs[1-6], symposia[7,8], and reviews[9-13]. Among the wide variety of organic compounds used as antioxidants, phenols and aromatic amines continue to attract most attention. In recent years, important new results were obtained in studies on the detailed mechanism of the action of these inhibitors. It was shown that the radicals formed from the inhibitor react with the hydrocarbons[14] and the hydroperoxide[15], thus participating in chain propagation. The exchange reactions between the radical of one inhibitor and the molecule of another play an important role[16]. The unique phenomenon of the regeneration of inhibitors in chain termination steps has been discovered[17]. The reactions of inhibitors with the hydroperoxide[18] and oxygen have been investigated[19,20]. The chemistry of stable free radicals

has developed rapidly[21-24] and extensive data on the reactions of peroxy-radicals with inhibitors have accumulated[25].

These new findings have made it necessary to revise the ideas about the mechanism of the inhibiting effect of phenols and amines, to analyse critically previous results and concepts, to compile data on elementary reactions involving oxidation inhibitors, and to formulate a mechanism of the action of inhibitors on the basis of modern results. Such an attempt is made in the present review.

II. STRENGTH OF THE In–H BOND IN PHENOLS AND AROMATIC AMINES

1. PHENOLS

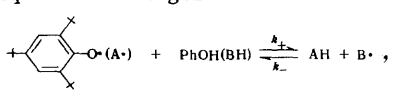
Peroxy-radicals react very rapidly with phenols[25]. At first sight, this can be explained by the low strength of the O–H bond. Therefore it is useful to examine the available data for the dissociation energy of the O–H bond in phenols ($D_{O\text{-}H}$). Several studies have been published recently in which quantities permitting the calculation of $D_{O\text{-}H}$ in phenols were determined by different methods.

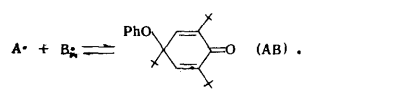
1. Mahoney et al.[26] determined calorimetrically the heat of the reaction

$$2PhO^{\cdot} + C_6H_5NHNHC_6H_5 \rightleftharpoons 2PhOH + C_6H_5NNC_6H_5$$

in benzene and found the difference $\Delta H_{PhO\cdot} - \Delta H_{PhOH}$ for certain stable phenoxy-radicals. Since $\Delta H_{PhOH} = \Delta H_{PhO\cdot} + \Delta H_H - D_{O\text{-}H}$, it follows that $D_{O\text{-}H} = \Delta H_{PhO\cdot} - \Delta H_{PhOH^+} + \Delta H_H$ and $\Delta H_H = 52.1$ kcal mole^{-1}. For tri-t-butylphenol, $\Delta H_{PhO\cdot} - \Delta H_{PhOH} = 29.14 \pm 0.08$ and $D_{O\text{-}H} = 29.1 \pm 52.1 = 81.2 \pm 0.1$ kcal mole^{-1}.

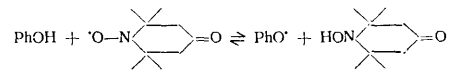
2. To measure the heat of formation of active phenoxy-radicals, a study was made[27] of the kinetics of the reaction between the tri-t-butylphenoxy-radical and various phenols and its heat was measured. The reaction includes two equilibrium stages:





The enthalpy of reaction is $\Delta\Delta H = -\Delta H_A + \Delta H_{AH} + \Delta H_B - \Delta H_{BH} + E_+' - E_-'$, the difference $\Delta H_A - \Delta H_{AH}$, measured by method 1 in chlorobenzene, is 28.25 ± 0.1 kcal mole^{-1}, E_-' was measured experimentally, and $E_+' \simeq 2$ kcal mole^{-1} since the recombination of phenoxy-radicals is rapid, its rate being limited by diffusion[27]; $D_{O\text{-}H} = \Delta\Delta H + E_-' + 78.3$ kcal mole^{-1}.

3. Vasserman et al.[28] and Kalashnikova et al.[29] measured the heats of the reversible reaction



and calculated from $D_{O\text{-}H}$ in hydroxylamine, which is 71.9 ± 3 kcal mole^{-1},[30] the values of $D_{O\text{-}H}$ for a number of phenols giving rise to stable phenoxy-radicals.

4. $D_{O\text{-}H}$ in phenols can be estimated from the activation energy for the reaction $PhOH + O_2 \xrightarrow{k_+} PhO^{\cdot} + HO_2^{\cdot}$. The reverse reaction $PhO^{\cdot} + HO_2^{\cdot} \xrightarrow{k_-} PhOH + O_2$ takes place in solution at a rate which is most probably diffusion-limited. This is supported by the finding that the rate of the analogous reaction $HO_2^{\cdot} + HO_2^{\cdot} \rightarrow HOOH + O_2$ in a hydrocarbon solution is limited by diffusion ($k \simeq 10^9$ litre mole^{-1} s^{-1}).[25] One can assume that $E_- = 1$ kcal mole^{-1} for the diffusion of $HO_2^{\cdot}$ in benzene, where k_+ was measured. The O_2 – H bond strength is 44–50 kcal mole^{-1}.[31] If we put $Q_{H\text{-}O_2} = 49$ kcal mole^{-1}, we obtain

$$q = E_- - E_+ = Q_{H\text{-}O_2} - D_{O\text{-}H} = E_+ + 48 \text{ kcal mole}^{-1}.$$

5. Hush[32] proposed a method for the estimation of $D_{O\text{-}H}$ from the critical oxidation-reduction potential[33], which can serve as a measure of the normal oxidation-reduction potential. The strength of the O–H bond in phenols is calculated from the formula[32] $D_{O\text{-}H} = FE_c + 57$ kcal mole^{-1}, where E_c is the critical potential in volts and $F = 23$ kcal equiv.$^{-1}$ V^{-1} is the Faraday. The results of the calculation of $D_{O\text{-}H}$ for phenols are presented in Table 1.

2. AROMATIC AMINES

The N–H bond dissociation energies in aromatic amines are unknown. $D_{N\text{-}H}$ can be estimated, as for phenols, from the activation energies for the reaction $InH + O_2 \rightarrow In^{\cdot} + HO_2$ (Denisova et al.[19]) by the formula $D_{N\text{-}H} = E + 48$ kcal mole^{-1}. It is also possible to estimate $D_{N\text{-}H}$ from the critical potentials for amines using the same formula as for phenols[32]: $D_{N\text{-}H} = FE_c + 57$ kcal mole^{-1}. The values of $D_{N\text{-}H}$ are presented in Table 2.

III. REACTION OF PEROXY-RADICALS WITH INHIBITORS

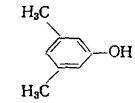
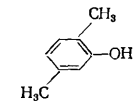
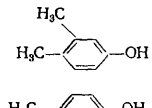
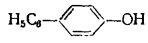
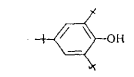
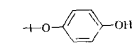
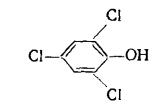
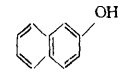
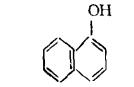
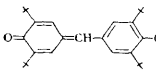
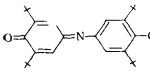
1. THE ISOTOPE EFFECT

If the peroxy-radical attacks the O–H bond of a phenol or the N–H bond of an amine, an isotope effect should be observed when hydrogen is replaced by deuterium. In a number of studies, where the inhibiting effect of phenols and aromatic amines on the oxidation of hydrocarbons was investigated[34-42], there was no isotope effect or it differed little from unity (1–1.3). A large isotope effect (10.6 for phenol at 65°C) was observed by Howard and Ingold[43] in the sensitised oxidation of styrene. The experimental difference between the activation energies[43] is $E_D - E_H = 1.1$ kcal mole^{-1}. Calculation yields a similar value[43]: $E_D - E_H = \frac{1}{2}h(\nu_{O\text{-}H} - \nu_{O\text{-}D}) = 1.36$ kcal mole^{-1}. The absence of an isotope effect in the reaction of $RO_2^{\cdot}$ and InH in the oxidation of other hydrocarbons can be accounted for by the formation of the hydroperoxide and rapid exchange via the reaction $InD + ROOH \rightleftharpoons InH + ROOD$. The oxidation of styrene yields a polymeric hydroperoxide which does not contain OOH groups and does not exchange hydrogen with the deuteriated inhibitor. An isotope effect was also observed for amines[44,45] and hydroxylamines[46] (Table 3).

2. THE REACTION MECHANISM

The isotope effect in experiments with deuteriated phenols and amines (Table 3) demonstrates convincingly that the rate-limiting stage in the reaction of $RO_2^{\cdot}$ with the inhibitor is the abstraction of a hydrogen atom: $RO_2^{\cdot} + InH \xrightarrow{k_7} ROOH + In$. The finding that phenolic ethers and tertiary aromatic amines do not exhibit an inhibiting effect is satisfactorily consistent with this mechanism. The molecular products of the reaction of inhibitors correspond

Table 1. The strength of O–H bonds in phenols.

Phenol	O–H bond strength, kcal mole^{-1}				
	method 1	method 2 C_6H_5Cl[27]	method 3 C_6H_6, C_7H_{16}[28,29]	method 4 C_6H_6[30]	method 5 C_7H_8OH — $-H_2O$[28,31]
1	2	3	4	5	6
C_6H_5OH	—	—	—	83±3	84
p-$NO_2C_6H_4OH$	—	—	—	—	90
m-$NO_2C_6H_4OH$	—	—	—	—	83
p-$CH_3C_6H_4OH$	—	—	—	80±3	81
m-$CH_3C_6H_4OH$	—	—	—	—	82
o-$CH_3C_6H_4OH$	—	—	—	—	81
p-t-$C_4H_9C_6H_4OH$	—	84.4±1	—	—	—
p-$CH_3OC_6H_4OH$	—	79.1±1	—	75±3	—
p-BrC_6H_4OH	—	85.8±1	—	—	—
m-$C_2H_5OCOC_6H_4OH$	—	87.2±1	—	—	—
	—	86.2±1	—	—	—
	—	—	—	—	81
	—	—	—	—	81
	—	—	—	—	81
	81.2±0.1	—	78.8±3*	—	—
	79.8±0.2	—	—	—	—
	—	84.9±1	—	—	82
	—	—	—	77±3	80
	—	—	—	73±3	75.4
	78.5±0.5	—	75.8±3	—	—
	77.7±0.5		76.0±3	—	—

* Kalashnikova et al.[29] obtained erroneously another value of D_{O-H} for hydroxylamine, namely 71.9 kcal mole^{-1}. The error arose because they employed in the calculation D_{O-H} for the >NO–H bond in 4-dihydroxy-2,2,6,6-tetramethylpiperidine (D = 65 kcal mole^{-1}), while they investigated the equilibrium between phenol and 2,2,6,6-tetramethyl-1-hydroxy-4-oxopiperidine (D = 71.9 kcal mole^{-1})[30].

to the following sequence of transformations (for further details, see Denisov and Emanuel'[9]):

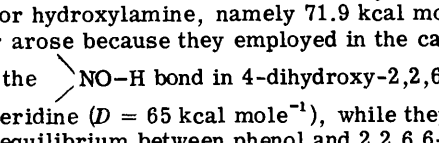


Table 2. Estimation of the N–H bond strengths in aromatic amines.

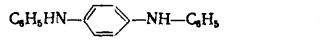
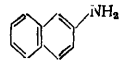
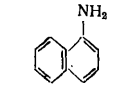
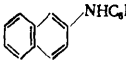
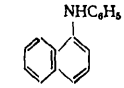
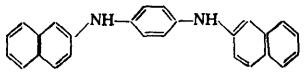
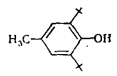
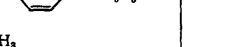
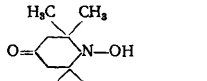
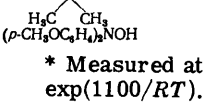
Amine	E_c, V (Ref.33)	D_{N-H}, kcal mole^{-1}	E(InH + O_2), kcal mole^{-1} (Ref.19)	D_N – H, kcal mole^{-1}
$C_6H_5NH_2$	1.135	88	—	—
$CH_3OC_6H_4NH_2$	0.892	77.5	—	—
p-$CH_3C_6H_4NH_2$	1.077	82	—	—
$C_6H_5NHCH_3$	1.053	81	—	—
$(C_6H_5)_2NH$	1.008	80	—	—
p-$(CH_3)_2NC_6H_4NH_2$	0.764	74.6	—	—
	0.710	73.3	—	—
	1.064	81.5	—	—
	0.841	76.3	30	78
	—	—	31	79
	—	—	32	80
	—	—	23	71

Table 3. The isotope effect in the reaction between $RO_2^{\cdot}$ and InH in styrene at 65°C.

Inhibitor	$(RO_2^{\cdot} + InH)$ litre mole^{-1} s^{-1}	k_H/k_D	References
	$2 \cdot 10^4$	10.6*	43
C_6H_5OH	—	~15	44
$(C_6H_5)_2NH$	$2 \cdot 10^4$	3.0	44
C_6H_5NH — β-$C_{10}H_7$	$5 \cdot 10^4$	3.0	44
C_6H_5NH — α-$C_{10}H_7$	$7 \cdot 10^4$	4.0	44
	—	3.0	45
$C_6H_5NHCH_3$	$4 \cdot 10^3$	3.0	45
	$5 \cdot 10^3$	3.0	46
	$5 \cdot 10^3$	2.0	46

* Measured at different temperatures: $k_H/k_D = 1.3 \exp(1100/RT)$.

a. The Polar Activated Complex $RO_2^{\cdot}$...H...In

Phenoxy-radicals react with phenols and amines, the corresponding rate constants being 10^4–10^6 litre mole^{-1}s^{-1} at 40–80°C. The question arises whether such high values of k_7 can be explained by the low strength of the In–H bond. We shall compare the values of k for the abstraction of H by the peroxy-radicals from tri-t-butylphenol (D_{O-H} = 81 kcal mole^{-1}, Table 1) and cumene (D_{C-H} = 76 kcal mole^{-1}): $\lg k\,(RO_2^{\cdot} + RH) = 6.51 - 10.13/\theta$ (Denisov[25]) and $\lg k\,(RO_2^{\cdot} + InH) = 6.58 - 3.4/\theta$ (Denisov[25]), where $\theta = 4.57 \times 10^{-3}\,T$. At 60°C, the ratio $k(RO_2^{\cdot} + InH)/k(RO_2^{\cdot} + RH) = 3 \times 10^4$. Thus the peroxy-radical

reacts with phenol 10^4 times faster than with cumene despite the fact that in cumene the C–H bond is somewhat weaker than the O–H bond of the phenol; the difference between the rate constants is associated with the difference between the activation energies. This can be explained by the markedly dipolar structure of the activated complex for the reaction between $RO_2^{\cdot}$ and InH, where the hydrogen atom is between two oxygen atoms (Fig. 1). Owing to the high electron affinity of oxygen atoms, a considerable proportion of the electron density of the O–H bond in the activated complex is located at the oxygen atom. The Coulombic attraction between $\overset{\delta-}{RO_2^{\cdot}}$, $\overset{\delta+}{H}$, and $\overset{\delta-}{OPh}$ causes a decrease of the potential barrier relative to that in the reaction between $RO_2^{\cdot}$ and RH. A similar situation obtains with aromatic amines, where the activated complex RO – O˙...H...N< is formed.

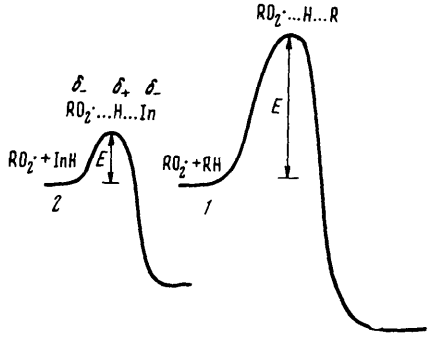


Figure 1. Schematic representation of the energy profiles for the reactions of the phenoxy-radicals with cumene (curve *1*) and ionol (curve *2*).

b. The $RO_2^{\cdot}$...HX Hydrogen Bond

Peroxy-radicals form a hydrogen bond of the type R'OO˙...HOR with the O–H group of water and alcohols[47–49]; this suggests that phenols and amines, which tend to form hydrogen bonds, react with peroxy-radicals via the preliminary formation of an association complex[50]:

$$RO_2^{\cdot} + InH \overset{k}{\rightleftharpoons} InH \ldots OOR \overset{k}{\rightarrow} In^{\cdot} + ROOH$$

Evidently the formation of the hydrogen bond between $RO_2^{\cdot}$ and InH increases the rate of reaction. It is not fortuitous that k_7 for the reaction of 2,6-dimethylphenol with the tetralylperoxy-radical[25] ($k_7 = 1.1 \times 10^4$ at 50°C) is higher than for the reaction involving 2,6-di-t-butylphenol[25] ($k_7 = 1.3 \times 10^3$): dimethylphenol forms a hydrogen bond with $RO_2^{\cdot}$, while di-t-butylphenol does not. In those cases where InH forms a hydrogen bond with the peroxy-radical, $k_7 = Kk$, $\Delta S_7^{\neq} = \Delta S_h + \Delta S^{\neq}$, $E_7 = E - Q_h$, and $\Delta H_7^{\neq} = \Delta H_h + \Delta H^{\neq}$, where the subscript h denotes a hydrogen bond. The quantity $K_{RO_2^{\cdot}\ldots HOPh}$ is unknown; for comparison, one can adduce K(phenol – dioxan) = 15.2 litre mole^{-1} in benzene at 25°C.[51]

3. DEPENDENCE OF k_7 ON THE STRUCTURE OF THE INHIBITOR.

The values of k_7 have been measured for a large number of phenols and amines[25] (the methods of measurement of k_7 have been described in a monograph[3]), but the vast majority of the measurements have been made at a single temperature. The activation energies for the reaction between $RO_2^{\cdot}$ and InH have been rarely measured. Table 4 shows that the values of E_7 are in the range 3.5–5.5 kcal mole^{-1}. However, one should bear in mind that the true activation energy for the reaction $RO_2^{\cdot}\ldots HIn \rightarrow ROOH + In^{\cdot}$ is higher and equal to $E_7 + \Delta H_h$ and ΔH_h = 3–4 kcal mole^{-1}. The rate constant k_7 is almost independent of the structure of the peroxy-radical of the hydrocarbon (Table 4).

Table 4. Rate constants for the reaction between $RO_2^{\cdot}$ and InH.

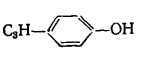
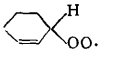
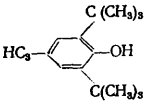
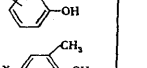
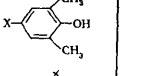
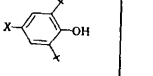
Inhibitor	$RO_2^{\cdot}$	Solvent	t, °C	lg k (litre mole^{-1} s^{-1})	lg A	E, kcal mole^{-1}	References
		cyclo-C_6H_{10}	49	3.88	7.02	4.5	52
ditto	$C_6H_5C(CH_3)_2OO\cdot$	$C_6H_5(CH_3)_2CH$	56	4.12	6.78	4.0	53
	~$CH_2(C_6H_5)CHOO\cdot$	$C_6H_5CH\text{-}CH_2$	40	4.00	7.92	5.6	54
ditto	$C_6H_5(CH_3)CHOO\cdot$	$C_6H_5C_2H_5$	60	4.34	6.58	3.4	55
α-$C_{10}H_7OH$	$C_6H_5(CH_3)CHOO\cdot$	$C_6H_5C_2H_5$	60	5.65	8.15	3.8	56
$(C_6H_5)_2NH$	$(CH_3)_2C(OO\cdot)CH_2CH\cdot(CH_3)_2$	$(CH_3)_2CHCH_2CH\cdot(CH_3)_2$	60	2.48	4.78	3.5	57

Table 5. Dependence of k_7 on the structure of the inhibitor.

InH	$RO_2^{\cdot}$	t°, C	Function	ρ	lg k_7, X=H	References
XC_6H_4OH	$C_6H_2(CH_3)_2COO\cdot$	62	σ	–3.7		35
ditto	$C_6H_5CH(OO\cdot)CH_2$~	65	σ+	–1.58	3.465	58
«	ditto	65	σ	–1.49	3.465	58
	»	65	σ+	–1.46	4.22	59
	»	65	σ+	–1.36	4.58	59
	»	65	σ+	–1.11	3.70	59
ditto		65	σ+	–1.36	3.89	60
$XC_6H_4NHCH_3$	$C_6H_5CH(OO\cdot)CH_2$	65	σ+	–1.6	3.60	45
$(XC_6H_4)_2NH$	ditto	65	σ+	–0.89	4.50	45

However, acylperoxy-radicals react with hydroquinone faster than do alkylperoxy-radicals[25]. Substituents in the benzene ring have a marked influence on the activity of the inhibitor: electropositive substituents increase and electronegative substituents decrease k_7. There is a linear correlation between $\lg k_7$ and σ^+ (Table 5).

4. EFFECT OF THE SOLVENT

When oxygen-containing compounds (H_2O, ROH, RCOOH, etc.) are added to the hydrocarbon, the rate of reaction of peroxy-radicals with the inhibitor decreases significantly[61-63]. This is primarily due to the formation of an intermolecular hydrogen bond In–H...Y, which blocks the susceptible O–H or N–H bond of the inhibitor and thus inhibits the reaction between $RO_2^\cdot$ and InH. In those cases where the solution contains the molecules of a hydroxy-compound (other than the inhibitor), the peroxy-radicals form with them a radical type hydrogen bond $RO_2^\cdot$...HOX, which causes additional inhibition of the reaction between peroxy-radicals and the inhibitor[62,63]. In the presence of compounds forming a hydrogen bond, we are dealing with the following series of stages in the inhibited oxidation reaction:

$$RO_2^\cdot + HIn \rightleftarrows RO_2^\cdot \ldots HIn \rightarrow ROOH + In^\cdot ,$$

$$InH + XOH \rightleftarrows InH \ldots O\begin{matrix}H\\X\end{matrix} ,$$

$$RO_2^\cdot + HOX \rightleftarrows RO_2^\cdot \ldots HOX ,$$

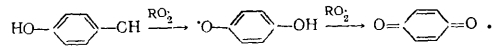
$$RO_2^\cdot \ldots HOX + InH \rightarrow ROOH + In^\cdot + HOX .$$

IV. REACTION OF In$^\cdot$ WITH $RO_2^\cdot$

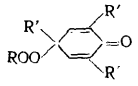
1. REACTION PRODUCTS

In the inhibited oxidation of hydrocarbons and polymers, free radicals (detected by ESR) are formed from the inhibitor. In the oxidation of octadecene at 171°C, a free radical (probably a nitroxide radical) is formed from phenyol-α-naphthylamine[64], its maximum experimental concentration being $[In^\cdot]_{max} \simeq 10^{-3}$ M for $[InH]_0 = 0.1$ M. A diphenylnitroxide radical is formed in the reaction of cumenylperoxy-radicals with diphenylamine[65]. Phenoxy-radicals have been detected in the oxidation of polypropylene by α-naphthol[66] {200°C, O_2 pressure 400 mmHg, $[In^\cdot]$ 10^{-5} M} and β-naphthol[66] {200°C, O_2 pressure 400 mmHg, $[In^\cdot]_{max} \simeq 2 \times 10^{-6}$ M}. The formation of labile coloured compounds was observed when the RH–O_2–amine system (diphenylamine, *N*-methylaniline, *NN'*-diphenyl-*p*-phenylenediamine)[67] was irradiated with electrons.

Molecular products are formed in the reaction of In$^\cdot$ radicals with $RO_2^\cdot$ and with one another. Hydroquinone is converted into quinone via the mechanism[68]:



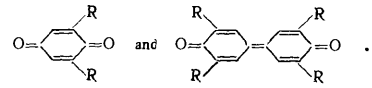
2,4,6-Trialkylphenols are converted into compounds of the type[69-71]



via the mechanism

$$InH \xrightarrow{RO_2^\cdot} In^\cdot \xrightarrow{RO_2^\cdot} ROOIn .$$

2,6-Dialkylphenol are converted into quinones[71-73]:



Diphenyl-*p*-phenylenediamine is converted quantitatively into quinonedi-imine[69], the reaction being analogous to that of hydroquinone.

2. THE STOICHIOMETRIC INHIBITION COEFFICIENT

The stoichiometric inhibition coefficient f is defined as the number of chains terminated by the inhibitor molecule and its reaction products under the given conditions. On the basis of the structures of the stable reaction products of hydroquinone, diphenyl-*p*-phenylenediamine, and 2,4,6-tri-t-butylphenol, one may conclude that $f = 2$ for these reference inhibitors. This permits the measurement of f for other inhibitors, by comparing the induction periods in initiated oxidation in the presence of the given and reference inhibitors. The values of f in cumene undergoing oxidation have been measured[69,74] and for the majority of phenols and aromatic amines proved to be close to two (the values of f are quoted in the author's handbook[25]).

3. REACTION OF THE DIPHENYLNITROGEN RADICAL WITH $RO_2^\cdot$

In the oxidation of cumene inhibited by diphenylamine, Thomas[65] detected a nitroxide radical by ESR. The same radical was also formed in cumene undergoing oxidation from a diphenylnitrogen radical (tetraphenylhydrazine served as a source of diphenylnitrogen radicals). Like diphenylamine, the diphenylnitroxide radical inhibits the oxidation of cumene, reacting with $RO_2^\cdot$ (the rate constant is 2.5×10^3 litre mole^{-1}s^{-1} at 68.5°C).[75] The ratio of the rate of formation of diphenylnitroxide radicals to the rate of initiation w_i is 0.11–0.19 for secondary peroxy-radicals and 0.20–0.33 for tertiary peroxy-radicals[76]. The following mechanism has been proposed for the reaction of diphenylamine (and other secondary amines) with peroxy-radicals[76,77]:

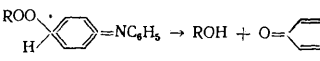
$$RO_2^\cdot + (C_6H_5)_2NH \rightleftarrows RO_2^\cdot \ldots HN(C_6H_5)_2 \rightarrow ROOH + (C_6H_5)_2N^\cdot ,$$

$$RO_2^\cdot + (C_6H_5)_2N \rightleftarrows ROON(C_6H_5)_2 \rightarrow [RO^\cdot + (C_6H_5)_2NO^\cdot] ,$$

$$[RO^\cdot + (C_6H_5)_2NO^\cdot] \rightarrow RO^\cdot + (C_6H_5)_2NO^\cdot ,$$

$$[RO^\cdot + (C_6H_5)_2NO^\cdot] \rightarrow \rangle C{=}O + (C_6H_5)_2NOH \text{ (for s-}RO_2^\cdot)$$

$$(C_6H_5)_2N^\cdot + RO_2^\cdot \rightarrow$$



This mechanism explains why the rate of formation of $(C_6H_5)_2NO^\cdot$ is always lower than w_i and why the ratio is smaller for secondary peroxy-radicals than for tertiary radicals. Diphenylnitroxide radicals terminate chains by reacting with $RO_2^\cdot$ and R$^\cdot$. The mechanism and the products of the reaction of $(C_6H_5)_2NO^\cdot$ and $RO_2^\cdot$ are so far unknown. Primary aromatic amines do not form oxides in reactions with peroxy-radicals[77]. It has been suggested that they give rise to nitroso-compounds[77]:

$$RO_2^\cdot + ArNH_2 \rightleftarrows ROO^\cdot \ldots HNHAr \rightarrow ROOH + ArN\dot{H} ,$$

$$ArN\dot{H} + ROO^\cdot \rightarrow [ArNHOOR] \rightarrow ArNO + ROH .$$

4. CHEMILUMINESCENCE IN THE REACTION OF $RO_2^{\cdot}$ WITH In$^{\cdot}$

In liquid-phase oxidation, chemiluminescence arises owing to the formation of excited molecules by the reaction between two peroxy-radicals[78]. This fact has served as a basis of the chemiluminescence methods for the investigation of oxidation reactions[78]. It was established recently that chemiluminescence can arise in liquid-phase oxidation in the presence of amines and polar molecules[79].

If an aromatic amine is added to cumene undergoing oxidation, the intensity of the luminescence decreases owing to the decrease in the rate of reaction between $RO_2^{\cdot}$ radicals. When an amine is added to cyclohexanol or chlorobenzene undergoing oxidation in the presence of t-butylalcohol and an initiator, the luminescence intensity increases despite the fall of $[RO_2^{\cdot}]$. Separate experiments showed that the decrease of luminescence is observed only in the presence of peroxy-radicals (initiator + O_2), aromatic amines, and polar (oxygen-containing) molecules (H_2O, ROH, R_2O). It was concluded that luminescence arises as a result of the reaction between peroxy-radicals and radicals generated from the aromatic amines. These are not nitroxide radicals, since luminescence is observed both with secondary amines (which give rise to nitroxide radicals) and with primary amines (which do not). Primary amines probably generate nitrogen radicals:

$$AmH + RO_2^{\cdot} \rightarrow Am^{\cdot} \xrightarrow{RO_2^{\cdot}} \Pi^{*} \rightarrow \Pi + h\nu$$

(only in the presence of polar molecules). The involvement of an amine radical in luminescence is confirmed by the finding that the addition of α-naphthol, which decreases $[Am^{\cdot}]$ owing to the reversible reaction

$$Am^{\cdot} + PhOH \rightleftharpoons AmH + PhO^{\cdot},$$

lowers the luminescence intensity. The occurrence of a new reaction generating chemiluminescence (in addition to the reaction between $RO_2^{\cdot}$ radicals) necessitates a very cautious approach to the employment of the chemiluminescence method for the investigation of the kinetics of the oxidation of organic compounds inhibited by amines and for the determination of its parameters.

V. REACTION OF INHIBITOR RADICALS WITH THE HYDROPEROXIDE

In a study of the effect of the hydroperoxide on the initiated oxidation of cumene in the presence of inhibitors, Thomas established[15] that the addition of the hydroperoxide accelerates the oxidation of cumene in the presence of phenol but has no influence if the oxidation of cumene is inhibited by 2,6-di-t-butylphenol and ionol. The experiments were performed at a low temperature (57.2°C) in the presence of azobisisobutyronitrile (8×10^{-3} M) when the additional initiation owing to the hydroperoxide was very insignificant. This can be accounted for by the reaction

$$PhO^{\cdot} + RO_2H \xrightarrow{k_{-7}} PhOH + RO_2^{\cdot},$$

as a result of which the concentration of peroxy-radicals increases in the presence of the hydroperoxide. The difference between the experiments with phenol and 2,6-di-t-butylphenol can be explained by the different reactivities of the phenoxy-radicals: a reactive phenoxy-radical is formed from phenol, while the 2,6-di-t-butylphenoxy-radical is relatively inactive and reacts slowly with the hydroperoxide. One can postulate the formation of a

Table 6. The reaction $In^{\cdot} + ROOH \rightarrow InH + RO_2^{\cdot}$ ($In^{\cdot}$ = )

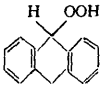
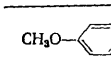
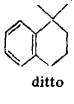
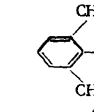
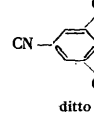
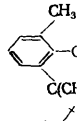
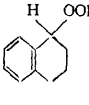
ROOH	Solvent	t, °C	lg k	References
$(CH_3)_3COOH$	CCl_4	0—21	6.33—8.3/θ	81
	C_6H_5Cl	24—60	4.11—5 8/θ	82
	C_6H_5Cl	24—60	5.60—8.6/θ	82

Table 7. The rate constant ratio k_{-7}/k_8 at 65°C in tetralin[83].

In$^{\cdot}$	ROOH	k_{-7}/k_8	k_{-7}, litre mole^{-1} s^{-1}
		$1.0 \cdot 10^{-6}$	$1.0 \cdot 10^{3}$
	ditto	$2.2 \cdot 10^{-5}$	$2.2 \cdot 10^{4}$
	»	$.6 \cdot 10^{-5}$	$2.6 \cdot 10^{4}$
m-$CH_3C_6H_4O^{\cdot}$	»	$3.7 \cdot 10^{-5}$	$3.7 \cdot 10^{4}$
$C_6H_5O^{\cdot}$	»	$5.2 \cdot 10^{-5}$	$5.2 \cdot 10^{4}$
ditto	$(CH_3)_3COOH$	$2.2 \cdot 10^{-5}$	$2.2 \cdot 10^{4}$
»	$C_6H_5(CH_3)_2COOH$	$2.2 \cdot 10^{-5}$	$2.2 \cdot 10^{4}$
»	$(C_6H_5)_3COOH$	$2.0 \cdot 10^{-6}$	$2.0 \cdot 10^{3}$
m-$CH_3OC_6H_4O^{\cdot}$		$2.3 \cdot 10^{-5}$	$2.3 \cdot 10^{4}$
p-Cl—$C_6H_4O^{\cdot}$	ditto	$2.8 \cdot 10^{-5}$	$2.8 \cdot 10^{4}$
	»	$1.7 \cdot 10^{-6}$	$1.7 \cdot 10^{3}$
	»	$9.2 \cdot 10^{-6}$	$9.2 \cdot 10^{3}$
ditto	$(CH_3)_3COOH$	$2.0 \cdot 10^{-6}$	$2.0 \cdot 10^{3}$
»	$C_6H_5(CH_3)_2COOH$	$2.0 \cdot 10^{-6}$	$2.0 \cdot 10^{3}$
»	$(C_6H_5)_3COOH$	$3.4 \cdot 10^{-7}$	$3.4 \cdot 10^{2}$
		$4.6 \cdot 10^{-7}$	$4.6 \cdot 10^{2}$
	ditto	$1.0 \cdot 10^{-8}$	10
	»	$4.9 \cdot 10^{-7}$	$4.9 \cdot 10^{2}$
ditto	$(CH_3)_3COOH$	$1.3 \cdot 10^{-7}$	$1.3 \cdot 10^{2}$
»	$C_6H_5(CH_3)_2COOH$	$1.5 \cdot 10^{-7}$	$1.5 \cdot 10^{2}$
»	$(C_6H_5)_3COOH$	$2 \cdot 10^{-8}$	20

* Calculated on the assumption that $k_8 = 10^9$ litre mole^{-1}s^{-1}.

hydrogen bond between phenol and the hydroperoxide, which should also retard the reaction between phenol and $RO_2^{\cdot}$:

$$PhOH + ROOH \rightleftharpoons PhOH \ldots \overset{H}{O}OR \quad \text{or} \quad PhOH \ldots \overset{OH}{O}R .$$

Calculation of the association constant from the relation between the rate of oxidation and [ROOH] yields an unreasonably large value of 300 litre mole^{-1} for the association constant of phenol with cumenyl hydroperoxide (at 57°C in cumene), while the same constant in carbon tetrachloride at 25°C is 12 litre mole^{-1} (determined from spectroscopic data). Evidently the hydrogen bond alone cannot account for this effect. A decrease of the relative overall rate constant for the reaction of the inhibitor with peroxy-radicals after the introduction of the hydroperoxide is observed also for aromatic amines[61]. As in the case of phenol, this is associated with the exchange reaction between the amine radical and the hydroperoxide (Denisov et al.[61] regarded this erroneously as a result of complex formation between the amine and the hydroperoxide).

The kinetics of inhibited oxidation in the presence of the hydroperoxide also demonstrate convincingly the occurrence of reaction between In$^{\cdot}$ and ROOH.

The inhibited oxidation of a hydrocarbon can be represented as follows taking into account the reaction between In$^{\cdot}$ and ROOH:

$$\text{initiator.} \rightarrow r^{\cdot} \xrightarrow{RH} R^{\cdot}, \quad (i)$$

$$R^{\cdot} + O_2 \rightarrow RO_2^{\cdot}, \quad (1)$$

$$RO_2^{\cdot} + RH \rightarrow ROOH + R^{\cdot}, \quad (2)$$

$$ROOH + RH \rightarrow RO^{\cdot} + H_2O + R^{\cdot}, \quad (3)$$

$$R^{\cdot} + R^{\cdot} \rightarrow R\text{–}R, \quad (4)$$

$$R^{\cdot} + RO_2^{\cdot} \rightarrow ROOR, \quad (5)$$

$$RO_2^{\cdot} + RO_2^{\cdot} \rightarrow \text{mol. products}, \quad (6)$$

$$RO_2^{\cdot} + InH \rightarrow ROOH + In^{\cdot}, \quad (7)$$

$$ROOH + In^{\cdot} \rightarrow RO_2^{\cdot} + InH, \quad (-7)$$

$$RO_2^{\cdot} + In^{\cdot} \rightarrow ROOIn . \quad (8)$$

At a fairly high partial pressure of oxygen when $[RO_2^{\cdot}] \gg [R^{\cdot}]$ and in the presence of an initiator when $W_i \gg k_3[ROOH][RH]$, reactions (3)–(5) may be disregarded. If the inhibitor radical is incapable of chain propagation owing to the reaction with the hydroperoxide, reaction (7) is responsible for chain termination and therefore $W_i = fk_7[InH][RO_2^{\cdot}]$; the rate of oxidation (for sufficiently long chains) is $W = k_2[RH]w_i/fk_7InH$, where k_2 refers to the reaction between $RO_2^{\cdot}$ and RH. When reaction (-7) is rapid $\{k_{-7}[ROOH][In^{\cdot}] \gg k_8[In^{\cdot}][RO_2^{\cdot}]$, k_8 refers to the reaction between $RO_2^{\cdot}$ and $In^{\cdot}\}$, chain termination is due to reaction (8), $W_i = 2k_8[In^{\cdot}][RO_2^{\cdot}]$, $k_7[InH][RO_2^{\cdot}] = k_{-7}[In^{\cdot}][ROOH]$, and $W = k_2[RH][RO_2^{\cdot}] = k_2[RH]\{k_{-7}W_i[ROOH]/2k_8k_7[InH]\}^{1/2}$. The experimental results are consistent with these formulae: for ionol in cumene[15] and tetralin[80] undergoing oxidation, $W \propto W_i/[InH]$, and for phenol in cumene[15] and tetralin[80], $W \propto \sqrt{W_i}/[InH]$. For phenol, the ratio $k_{-7}/k_8 = 5.7 \times 10^{-5}$ in cumene[15] at 57.2°C and $k_{-7} = 2.3 \times 10^5$ litre mole^{-1}s^{-1}, i.e. is very high. The values of k_{-7} are listed in Tables 6 and 7.

VI. CHAIN PROPAGATION VIA THE REACTION OF In$^{\cdot}$ WITH THE HYDROCARBON

Phenoxy-radicals can abstract a hydrogen atom not only from the hydroperoxide but also from hydrocarbons. If the phenoxy-radical is reactive and the hydrocarbon has a fairly weak C–H bond, such a reaction will be comparatively fast and will affect the retarding action of the inhibitor. Bickel and Kooyman[14], who studied the kinetics of the inhibited oxidation of 9,10-dihydroanthracene, established that the relation $W/[InH]^{1/2} = C_1 + C_2[InH]$, which is consistent with the involvement of In$^{\cdot}$ in chain propagation via the reaction with the hydrocarbon, holds for 4-t-butyl-2,6-dimethylphenol. In a study of the sensitised oxidation of tetralin in the presence of phenols, Mahoney and Ferris[84] established the following relation between the rate of oxidation and the concentrations of phenol, the hydrocarbon, and the initiator: $w = \text{const.}\,[RH]^{3/2}[C_6H_5OH]^{-\frac{1}{2}}[\text{initiator}]^{\frac{1}{2}}$. This relation agrees satisfactorily with the oxidation mechanism involving reactions (i) and (1)–(6) and the following reactions involving the inhibitor:

$$RO_2^{\cdot} + InH \rightarrow ROOH + In^{\cdot}, \quad (7)$$

$$RO_2^{\cdot} + In^{\cdot} \rightarrow ROOIn, \quad (8)$$

$$In^{\cdot} + In^{\cdot} \rightarrow In\text{—}In, \quad (9)$$

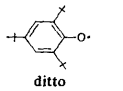
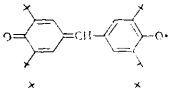
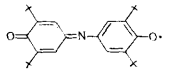
$$In^{\cdot} + RH \rightarrow InH + R^{\cdot} . \quad (10)$$

According to this mechanism, the rate of oxidation for $k_9[In^{\cdot}] \ll k_8[RO_2^{\cdot}]$ is

$$W = k_2\left(\frac{k_{10}w_i}{2k_7k_8}\right)^{1/2}[RH]^{3/2}[InH]^{-1/2} .$$

The constants k_{10} for stable phenoxy-radicals are listed in Table 8.

Table 8. Rate constants for the reaction In$^{\cdot}$ + RH → InH + R.

In	RH	t°,C	$\lg k$, $\theta = 4.57 \cdot 10^{-3}T$	References
	n-$C_{10}H_{22}$	120—150°	10.415—27.5, θ	
ditto	$(CH_3)_2CH(CH_2)_7CH_3$	90—150	9.28—25.5/θ	85
»	$C_6H_5CH_3$	100—150	8.78—23.0/θ	
»	$C_6H_5C_2H_5$	70—100	5.43—17.0/θ	
»	$C_6H_5CH(CH_3)_2$	100—160	4.69—16.5/θ	
»	$(C_6H_5)_2CH_2$	80—150	5.08—14.5/θ	
	$C_6H_5C_2H_5$	60—140	3.255—14.0/θ	86
	$C_6H_5C_2H_5$	80—130	3.48—14.8/θ	86

In 1955 Hammond et al.[35] established that the rate of oxidation of cumene in the presence of phenol and *N*-methylaniline is directly proportional to $\{[\text{initiator}]/[InH]\}^{\frac{1}{2}}$. On this basis, they proposed the following mechanism for chain termination involving the inhibitor:

$$RO_2^{\cdot} + InH \rightleftharpoons RO_2^{\cdot} \ldots InH ,$$

$$RO_2^{\cdot} + RO_2^{\cdot} \ldots InH \rightarrow ROOH + ROOIn .$$

This mechanism accounts for the relation $W \propto \{W_i/[InH]\}^{\frac{1}{2}}$ but it is inconsistent with the isotope effect for deuterium-substituted phenols and amines and the absence of an inhibiting effect of phenolic ethers and tertiary amines. There is also a difference between the kinetic relations which follow from the Boozer–Hammond mechanism and the mechanism involving In$^{\cdot}$ in chain propagation. According to the Boozer–Hammond mechanism, $W \propto [RH]$, while according to the mechanism involving reactions (7), (8), and (10), $W \propto [RH]^{3/2}$. The latter relation is in fact observed experimentally[35]. Therefore the mechanism involving the reaction between In$^{\cdot}$ and RH must be regarded as valid for phenols and amines in hydrocarbons undergoing oxidation; the Boozer–Hammond mechanism does not obtain in hydrocarbons in the presence of phenols and amines.

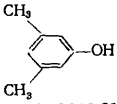
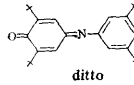
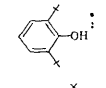
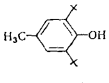
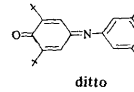
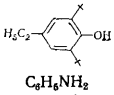
VII. THE EXCHANGE REACTION $In_1^{\cdot} + In_2H \rightleftharpoons In_1H + In_2^{\cdot}$

1. AMINE + PHENOL

In a study of the combined action of β-naphthylphenylamine and 2,6-di-t-butylphenol on the oxidation of ethylbenzene, Karpukhina et al.[16] established an interesting fact: if the phenol is present in a hydrocarbon undergoing oxidation, the amine is hardly consumed, a rapid decrease of its concentration in the oxidation process beginning only after the phenol has been used up. This finding cannot be accounted for by the fact that the amine reacts with peroxy-radicals more slowly than the phenol. On the contrary, for the amine $k_7 = 1.3 \times 10^5$ litre mole^{-1}s^{-1}, while for the phenol $k_7 = 0.95 \times 10^4$ litre mole^{-1}s^{-1} (ethylbenzene, 60°C). The unusual kinetics of the consumption of the amine in the presence of the phenol can be explained by the reaction $Am^{\cdot} + PhOH \rightleftharpoons AmH + PhO^{\cdot}$. The reaction has been demonstrated in experiments with tetraphenylhydrazine[16]. The dissociation of tetraphenylhydrazine results in the formation of diphenylnitrogen radicals, which are converted into diphenylamine in the presence of ionol. In the absence of the phenol, very little diphenylamine is formed. The exchange reaction between Am$^{\cdot}$ and PhOH leads to a synergic effect: a mixture of the amine and the phenol gives rise to more prolonged inhibition of the oxidation of ethylbenzene at 120°C than either inhibitor separately[87–91].

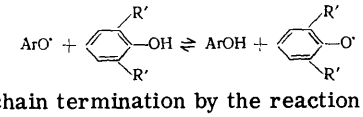
This can be explained by the fact that the amine gives rise to a radical capable of chain propagation by reaction with the hydrocarbon. Therefore the inhibition of the oxidation by the amine is incomplete despite the high rate constant k_7. The dialkylphenol forms relatively inactive phenoxy-radicals incapable of chain propagation, but it reacts with peroxy-radicals more slowly than does the amine. The rapid exchange reaction between Am$^{\cdot}$ and ArOH makes it possible to combine two valuable properties, namely the rapid chain termination by the reaction of $RO_2^{\cdot}$ with the amine and the inactivity of ArO$^{\cdot}$ in chain propagation reactions. β-Naphthylphenylamine is not consumed in oxidation in the presence of phenols giving rise to inactive phenoxy-radicals and the equilibrium $Am^{\cdot} + PhOH \rightleftharpoons AmH + PhO^{\cdot}$ is displaced to the right. Investigation showed that this is true of 2,6-dialkylphenols, while in the case of *p*-substituted and mono-*o*-substituted phenols the effect of the replacement of Am$^{\cdot}$ by PhO$^{\cdot}$ is absent[55,91]. *p*-Phenylenediamine and also hydroxy-derivatives of diphenylamine and β-naphthylphenylamine likewise fail to give rise to this type of effect[92] (apparently the Am$^{\cdot}$ radicals derived from these amines are relatively inactive).

Table 9. Rate constants for the reaction ArO$^{\cdot}$ + In$^{\cdot}$H → ArOH + In$^{\cdot}$.

ArO$^{\cdot}$ radical	InH	Solvent	t°C	lg k (litre mole^{-1} s^{-1})	References
	C_6H_5OH	C_6H_6	25—60	4.85— 5 5/0	82
ditto	C_6H_5OH	C_6H_6	24	0 49	81
»	o-$NO_2C_6H_4OH$	C_6H_6	20—90	4.78—12.1/0	93
»	p-$(CH_3)_3CC_6H_4OH$	C_6H_6	25—60	5.88— 5.3/0	93
»	p-$CH_3OC_6H_4OH$	C_6H_6	25	3.28	82
»	p-$CH_3OC_6H_4OH$	C_6H_6	24	3.48	94
»	p-$C_6H_5C_6H_4OH$	C_6H_6	24	2.10	
»	p-$(CH_3)_3CC_6H_4OH$	C_6H_6	24	1.66	
»	p-BrC_6H_4OH	C_6H_6	24	0.64	
»	p-$CH_3OCOC_6H_4OH$	C_6H_6	24	1.32	
»	p-CNC_6H_4OH	C_6H_6	24	1.88	
»	$(CH_3)_3CC_6H_4OH$	C_6H_6	24	1.02	
»		C_6H_6	24	1.19	94
»	m-$C_2H_5OCOC_6H_4OH$	C_6H_6	24	1 78	
»	m-CNC_6H_4CH	C_6H_6	24	2.90	
»	m-$ClC_6H_4NH_2$	CCl_4	23.5	0.60	81
»	C_6H_5NH-β-$C_{10}H_7$	$C_6H_5C_2H_5$	—30—23	4.61—4.0/0	55
	C_6H_5OH	o-$CH_3C_6H_4CH_3$	30—50	6.49—10.5/0	
ditto	p-$CH_3C_6H_4OH$	ditto	30	2.90	
»	p-$NO_2C_6H_4OH$	»	30	2.90	
»		»	30	0.49	95
»		»	30—50	3.84—5 5/0	
		o-$CH_3C_6H_4CH_3$	30	1.74	
ditto	$C_6H_5NH_2$	ditto	30—50	3.85—7.3/0	
»	$(C_6H_5)_2NH$	»	30—50	1.30—6.4/0	
»	$(p$-$NO_2C_6H_4)_2NH$	»	50	3.38	95
»	$(m$-$NO_2C_6H_4)NH$	»	50	3,32	
»	$(o$-$NO_2C_6H_4)_2NH$	»	50	3.90	

2. PHENOL + PHENOL

An analogous exchange mechanism was investigated by Mahoney[94] in mixtures of two inhibitors, one of which was a 2,6-dialkylphenol and the other a phenol with a substituent in the *para*-position. A 2,6-dialkylphenol reacts with $RO_2^{\cdot}$ relatively slowly, but it gives rise to inactive radicals. A phenol with a substituent in the *para*-position reacts rapidly with $RO_2^{\cdot}$, but the phenoxy-radical formed from it is reactive and can cause chain propagation by reaction with the hydrocarbon (if the latter has a weak C–H bond) and with the hydroperoxide (see above). When two such phenols are introduced sumultaneously, the rapid exchange process (equilibrium displaced to the right)



causes fast chain termination by the reaction of $RO_2^{\cdot}$ and ArOH, while the ArO$^{\cdot}$ radicals take little part in chain propagation reactions, since they undergo rapid exchange for the inactive 2,6-dialkylphenoxy-radicals. The rate constants for the exchange reactions involving phenoxy-radicals are listed in Table 9.

VIII. REACTION OF THE INHIBITOR WITH THE HYDROPEROXIDE

Rapid chain termination by inhibitors (phenols and aromatic amines) is due to the fact that the peroxy-radical is a powerful oxidant and the inhibitors are reductants. Another oxidant (the hydroperoxide), which can react with the inhibitor, is formed and is present, apart from $RO_2^{\cdot}$, in organic compounds undergoing oxidation. If its reaction with the inhibitor results in the formation of molecular products only, it leads merely to an additional consumption of the inhibitor. If it involves the formation of free radicals, it can serve as an additional source of initiation. This must be borne in mind in the analysis of the mechanism of the inhibited oxidation of hydrocarbons and polymers.

The reaction of phenols with cumenyl hydroperoxide was investigated in chlorobenzene solution[18]. The rate of reaction is $w = k[\mathrm{PhOH}][\mathrm{ROOH}]$. It results in the formation of radicals, which initiate the oxidation. This has been demonstrated in experiments on the oxidation of cumene with the hydroperoxide and *p*-methoxyphenol.

Under these conditions, the oxidation mechanism in the absence of an initiator includes reactions (1)–(6) and the following reactions with the inhibitor:

$$\mathrm{InH} + \mathrm{RO_2^{\cdot}} \rightarrow \mathrm{In^{\cdot}} + \mathrm{ROOH}\,, \qquad (7)$$

$$\mathrm{ROOH} + \mathrm{In^{\cdot}} \rightarrow \mathrm{RO_2^{\cdot}} + \mathrm{InH}\,, \qquad (-7)$$

$$\mathrm{In^{\cdot}} + \mathrm{RO_2^{\cdot}} \rightarrow \mathrm{InOOR}\,, \qquad (8)$$

$$\mathrm{InH} + \mathrm{ROOH} \rightarrow \mathrm{In^{\cdot}} + \mathrm{H_2O} + \mathrm{RO^{\cdot}}\,. \qquad (11)$$

The radicals formed by reaction (11) are partly destroyed in the cage and are partly released into the bulk phase, so that the rate constant for initiation owing to this reaction is $k_{i11} = 2ek_{11}$, where e is the probability of the release of the radicals into the bulk phase. The rate of oxidation $W = k_2[\mathrm{RH}][\mathrm{RO_2^{\cdot}}]$,

$$[\mathrm{RO_2^{\cdot}}] \simeq \sqrt{\frac{k_{-7}[\mathrm{ROOH}]^2 W_i}{2k_7 k_8 [\mathrm{InH}]}};\quad W_i = 2k_3[\mathrm{ROOH}][\mathrm{RH}] + 2ek_{11}[\mathrm{ROOH}][\mathrm{InH}]\,,$$

and

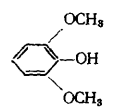
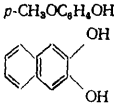
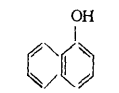
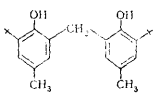
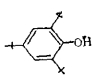
$$\frac{W^2[\mathrm{InH}]}{[\mathrm{ROOH}]^3} = \frac{k_2^2[\mathrm{RH}]^2 k_{-7}}{2k_7 k_8}\cdot(2k_3[\mathrm{RH}] + 2ek_{11}[\mathrm{InH}])\,.$$

This type of relation is in fact observed experimentally, which indicates the formation of radicals in the reaction between the phenol and the hydroperoxide. By comparing k_{11} (determined from the rate of decomposition of the hydroperoxide) with k_{i11} {determined from the relation between W and [InH]}, $e = 0.27$ at 120°C was found. The formation of phenoxy-radicals in the reaction between ROOH and the phenol was demonstrated by the ESR method for tri-t-butylphenol. For sterically hindered phenols, it is reasonable to postulate the formation of a hydrogen bond between the phenol and the hydroperoxide. The reaction mechanism is as follows:

$$\mathrm{ROOH} + \mathrm{PhOH} \overset{K}{\rightleftharpoons} \mathrm{ROO}\cdots\overset{\mathrm{H}}{\underset{\mathrm{HOPh}}{}} \xrightarrow{k} [\mathrm{RO^{\cdot}} + \mathrm{H_2O} + \mathrm{PhO^{\cdot}}] \rightarrow \mathrm{RO^{\cdot}} + \mathrm{H_2O} + \mathrm{PhO^{\cdot}} \quad \mathrm{mol.\ products}\,.$$

The experimental rate constant $k_{11} = Kk$, where K is the effective equilibrium constant (one must bear in mind that the phenol and the hydroperoxide forms several hydrogen-bonded association complexes, of which only one reacts). The rate constant k_{11} depends very markedly on the structure of the phenol (Table 10). The reaction between amines and peroxides has been discussed in a review[13].

Table 10. Rate constants for the reactions of phenols with cumenyl hydroperoxide[18] (solvent—chlorobenzene and n-decane in experiments with 2,4,6-tri-t-butylphenol).

Phenol	k_{11} at 140°C, litre mole^{-1} s^{-1}	E, kcal mole^{-1}	lg$A$ (litre mole^{-1} s^{-1})
	$6.5\cdot10^{-3}$	22.9±1.1	9.91±0.63
p-$CH_3OC_6H_4OH$	$4.3\cdot10^{-3}$	23.3±1.4	9.95±0.78
	$4.5\cdot10^{-3}$	25.8±0.8	11.33±0.45
	$6.7\cdot10^{-4}$	24.2±1.0	9.63±0.89
	$4.2\cdot10^{-4}$	26.0±0.7	10.36±0.42
p-$CH_3C_6H_4OH$	$2.0\cdot10^{-4}$	26.2±2.0	10.15±1.11
	$7.8\cdot10^{-5}$	25.9±1.0	9.60±0.54

The hypothesis has been put forward[96] that the inhibitor is involved in degenerate chain branching via its interaction with a pair of radicals in a solvent (or polymer) cage. On decomposition of the hydroperoxide by the reaction

$$\mathrm{ROOH} + \mathrm{RH} \rightarrow \mathrm{RO^{\cdot}} + \mathrm{H_2O} + \mathrm{R^{\cdot}}$$

or as a result of the consecutive reactions

$$\mathrm{ROOH} \rightarrow \mathrm{RO^{\cdot}} + \mathrm{HO^{\cdot}},\quad \mathrm{HO^{\cdot}} + \mathrm{RH} \rightarrow \mathrm{H_2O} + \mathrm{R^{\cdot}},$$

one cage contains both RO$^{\cdot}$ and R$^{\cdot}$ radicals. Some of these pairs recombine and some are released into the bulk phase. It is suggested that the inhibitor in the cage reacts with one of the radicals and thereby increases the probability of liberation of the radicals from the cage. A bifunctional inhibitor allegedly reduces the probability of the release of the radicals into the bulk phase by reacting with two radicals. However, in order to influence the liberation of the radicals from the cage (to increase or decrease the probability), the inhibitor must compete successfully with the diffusion of the radicals from the cage. In the usual solvents with low viscosity (benzene, heptane, etc.), the rate constants for the diffusion of molecules and radicals at about 20°C are very high (10^9–10^{10} litre mole^{-1}s^{-1}). The concentration of the inhibitor is usually low (10^{-4}–10^{-2} M). Therefore the specific rate of diffusion of the radical from the cage is always much higher than the rate of its reaction with the inhibitor even when the rate constant for this reaction is large {$k_7 \simeq 10^7$ litre mole^{-1}s^{-1}, $k_D \gtrsim 10^9$, $k_7[\mathrm{InH}] \lesssim 10^5$}.

Experiment confirmed this conclusion. Waits and Hammond[97] investigated the decomposition of the dinitrile of azocyclohexanecarboxylic acid in the presence of active acceptors of alkyl radicals such as I_2, Br_2, and diphenylpicrylhydrazyl, which react with alkyl radicals, the rate constant being close to k_D. It was established that free radical acceptors do not influence the yield of recombination products within the cage up to a concentration of 0.1 M. In a viscous medium (a polymer melt) at a high temperature (180°C and above), rapid release of radicals into the bulk phase from the cage is insured by intense segmental diffusion (if two macroradicals are formed).

The inhibitor has no influence on the initiation efficiency in the solid phase either, as shown by measurements of the rate of consumption of inhibitors (α-naphthol, α-naphthylamine) in polyethylene and polystyrene when the radicals are generated from azobisisobutyronitrile. Thus the hypothesis of the involvement of the inhibitor in initiation via the reaction of radicals in the cage is contrary to both experimental facts and theoretical estimates.

IX. REACTION OF THE INHIBITOR WITH OXYGEN

Phenols and aromatic amines react with molecular oxygen bimolecularly[19,20]:

$$InH + O_2 \rightarrow In^{\cdot} + HO_2^{\cdot}$$

The activation energy for this reaction is close to its endothermicity, which makes it possible to estimate the strength of the weakest bond in the inhibitor from the value of E (Tables 1 and 2). The pre-exponential factor varies over the range 10^9–10^{12} litre mole^{-1}s^{-1} (Table 11), i.e. is fairly close to the frequency factor for binary collisions in a liquid. According to the collision theory, in a liquid[93] $A = KP(6\nu/z)E/RT$, where P is the steric factor, ν the molecular vibration frequency in the liquid, z the number of neighbouring molecules surrounding the reacting molecules, E the activation energy, and K the equilibrium constant for the reaction $RH + O_2 = [RH + O_2]$. Hence we have $A = 2 \times 10^{14} P$ for $\nu = 10^{13}$ s^{-1}, $z = 12$, $E = 30$ kcal mole^{-1}, $K = 1$ litre mole^{-1}, and $T = 400$°K; when $A = 2 \times 10^{11}$, $P = 10^{-3}$.

Table 11. Rate constants for the reaction of InH with O_2 in benzene[19,20].

Inhibitor	k at 180°C, litre mole^{-1} s^{-1}	E, kcal mole^{-1}	lg$A$ (litre mole^{-1} s^{-1})
C_6H_5OH	$0.9 \cdot 10^{-4}$	35	12.845
p-$CH_3C_6H_4OH$	$1.2 \cdot 10^{-4}$	32	11.48
p-$CH_3OC_6H_4OH$	$7.4 \cdot 10^{-4}$	27	9.875
β-$C_{10}H_7OH$	$4.5 \cdot 10^{-4}$	29	10.65
α-$C_{10}H_7OH$	$2.0 \cdot 10^{-3}$	25	9.34
α-$C_{10}H_7NHC_6H_5$	$1.7 \cdot 10^{-5}$	32	10.545
β-$C_{10}H_7NHC_6H_5$	$5.6 \cdot 10^{-5}$	31	10.46
α-$C_{10}H_7NH_2$	$6.0 \cdot 10^{-5}$	30	10.175
β-$C_{10}H_7$—NH——NH—β-$C_{10}H_7$	$1.4 \cdot 10^{-2}$	23	9.145

It has been suggested[99,100] that the reaction of the inhibitor with oxygen is the main source of initiation in the induction period of the inhibited oxidation process. The finding[99] that in polypropylene undergoing oxidation α-naphthol was consumed in a first-order reaction and the specific rate of its consumption increased with oxygen pressure supported this hypothesis. In the initial period of the oxidation reaction, initiation is due to reactions involving oxygen: $RH + O_2 \rightarrow R^{\cdot} + HO_2^{\cdot}$ and $2RH + O_2 \rightarrow 2R^{\cdot} + H_2O_2$. The reaction between InH and O_2 plays a significant role if its rate is comparable to (or higher than) the rate of chain initiation w_0. Comparison of the experimental values of w_0 with the rate of reaction between InH and O_2 shows that, even for a comparatively active inhibitor such as α-naphthol, $W_0 \gg W(InH + O_2)$ in polymers undergoing oxidation.

Indeed in polyethylene at 118°C and an oxygen pressure of 1 atm, $W_0 = 1.5 \times 10^{-7}$ mole kg^{-1} s^{-1} and the rate of reaction of α-naphthol with oxygen for $[InH] = 10^{-3}$ mole kg^{-1} is approximately 2×10^{-11} mole kg s^{-1}; in polypropylene at 130°C and an oxygen pressure of 1 atm, $W_0 = 2.4 \times 10^{-6}$ mole kg^{-1} s^{-1} and $W(InH + O_2) \simeq 6 \times 10^{-11}$ mole kg^{-1} s^{-1} {[α-naphthol] = 10^{-3} mole kg^{-1}}.

X. REGENERATION OF THE INHIBITOR IN CHAIN TERMINATION STEPS

Chain termination in the reaction between the peroxy-radical and the inhibitor is accompanied by destruction of the latter. For the vast majority of phenols and amines, the stoichiometric inhibition coefficient[25] is close to two, which can be accounted for by the following chain termination mechanism:

$$RO_2^{\cdot} + InH \rightarrow ROOH + In^{\cdot},$$
$$RO_2^{\cdot} + In^{\cdot} \rightarrow \text{mol. products}.$$

In a study of the oxidation of cyclohexanol[101], it was established that α-naphthylamine inhibiting the initiated oxidation of cyclohexanol is consumed at a rate smaller by a power of several tens than the rate of initiation. An analogous phenomenon is observed in the oxidation of other secondary and primary alcohols[102] and is characteristic not only of α-naphthylamine but also of other aromatic amines. This phenomenon is due to the regeneration of the aromatic amine in the alcohol undergoing oxidation and the repeated involvement of a single amine molecule in chain termination. The mechanism of the regeneration of the amine was discovered by Kharitonov and Denisov[103], who established the formation of diphenylamine from the diphenylnitrogen radical in cyclohexanol undergoing oxidation. Chain propagation in an alcohol undergoing oxidation is due to the hydroxyperoxy-radical $\rangle C(OH)OO^{\cdot}$, which exhibits a dual reactivity: it can oxidise by abstracting a hydrogen atom from the molecule via its peroxy-group and it can reduce the radical by giving up to it the hydrogen atom from its hydroxy-group. The latter reaction leads to the regeneration of the inhibitor and irreversible destruction of the latter takes place as a result of the reaction of the radical In$^{\cdot}$ with the peroxy-group of the hydroxy-peroxy-radical:

$$\rangle C(OH)OO^{\cdot} + InH \xrightarrow{k_7} \rangle C(OH)OOH + In^{\cdot},$$
$$\rangle C(OH)OO^{\cdot} + In^{\cdot} \xrightarrow{k_8'} InH + O_2 + \rangle C{=}O,$$
$$\rangle C(OH)OO^{\cdot} + In^{\cdot} \xrightarrow{k_8} InOO(HO)C \rightarrow \text{products}.$$

The degree of regeneration of the amine depends on the ratio of the rate constants for reactions (8) and (8′): $f = w_i/w_{InH}$; the rate of initiation w_i is equal to the rate of

chain termination, i.e. $w_i = \{k_7[InH] + (k_8 + k_8')[In^\cdot]\}[RO_2^\cdot]$ and $w_{InH} = k_7[InH][RO_2^\cdot] - k_8'[In^\cdot][RO_2^\cdot]$, whence we find

$$f = \frac{k_7[InH] + (k_8 + k_8')[In^\cdot]}{k_7[InH] - k_8'[In^\cdot]}, \quad [In^\cdot] = \frac{k_7[InH]}{k_8 + k_8'}, \quad f = 2\left(1 + \frac{k_8'}{k_8}\right) .$$

The mechanism of the regeneration of α-naphthylamine in cyclohexanol undergoing oxidation was investigated recently in greater detail[104]. In an alcohol undergoing oxidation, chain termination takes place via the reactions:

$$\rangle\dot{C}OH + O_2 \xrightarrow{k_1} \rangle C(OH)OO^\cdot ,$$
$$\rangle C(OH)OO^\cdot + \rangle CHOH \xrightarrow{k_2} \rangle C(OH)OOH + \rangle\dot{C}OH .$$

The hydroxyhydroperoxide formed decomposes into a ketone and hydrogen peroxide, the latter generating hydroperoxy-radicals by reaction with hydroxyperoxy-radicals:

$$\rangle C(OH)OOH \rightleftharpoons \rangle C{=}O + H_2O_2 ,$$
$$H_2O_2 + \rangle C(OH)OO^\cdot \rightarrow HO_2^\cdot + \rangle C(OH)OOH$$

Therefore an alcohol undergoing oxidation contains simultaneously hydroxyalkyl, hydroxyperoxy-, and hydroperoxy-radicals, each of which can reduce In$^\cdot$ to InH. To confirm the role that each of these radicals plays in the regeneration of α-naphthylamine, a study was made of the relation between f in an alcohol undergoing oxidation on the one hand and the partial pressure of oxygen and the concentration of hydrogen peroxide on the other. Since hydroxyalkyl radicals are consumed by the reaction with oxygen and are formed by reaction (2), their steady-state concentration is inversely proportional to the concentration of dissolved oxygen:

$$[\rangle\dot{C}OH] = \frac{k_2}{k_1}\frac{[\rangle CHOH]}{[O_2]}[\rangle C(OH)OO^\cdot] .$$

By changing $[O_2]$, it is possible to follow the regeneration of the inhibitor by the reaction with hydroxyalkyl radicals. In the absence of oxygen, the regeneration can be achieved only by hydroxyalkyl radicals. In the experiments of Bardanyan et al.,[104] measurements were made of the rate of consumption of α-naphthylamine in cyclohexanol being oxidised at 120°C with $W_i = 1.86 \times 10^{-6}$ mole litre^{-1}s^{-1} and $[InH] = 8 \times 10^{-4}$ M at different partial pressures of oxygen. The experimental results[104] are presented below:

Partial oxygen pressure	= 0	61	160	300	760 mmHg.
f =	16.6	25	36	44	48

It is evident from these data that the degree of regeneration of the amine in the reaction with peroxy radicals is higher than in the reaction with hydroxyalkyl radicals and that the role of hydroxyalkyl radicals in regeneration at atmospheric oxygen pressure is insignificant. (Calculation shows that 95% of In$^\cdot$ is converted into InH as a result of the reaction with peroxy-radicals at an oxygen pressure of 1 atm.)

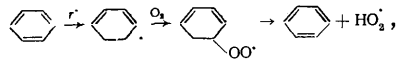
Experiments with different concentrations of hydrogen peroxide in cyclohexanol at 75°C and with $W_i = 3.7 \times 10^{-7}$ mole litre^{-1}s^{-1} showed that, as $[H_2O_2]$ increases, the coefficient f diminishes from $f = 90$ in pure cyclohexanol to $f = 20$ for $[H_2O_2] \geq 0.08$ M. Consequently hydroperoxy-radicals also reduce In$^\cdot$ to InH, but in this case k_8'/k_8 is significantly lower than for hydroxyperoxy-radicals. With increased concentration of hydrogen peroxide in the alcohol undergoing oxidation, the role of $HO_2^\cdot$ radicals in the regeneration of the inhibitor becomes more pronounced. The following values of k_8'/k_8, characterising the relative capacity of various radicals to regenerate the inhibitor, were obtained from experimental data for α-naphthylamine in cyclohexanol at 75°C: 47 ± 5 for the hydroxyperoxy-radical, 9 ± 2 for the hydroperoxy-radical, and 6 ± 2 for the hydroxyalkyl radical. The regeneration is characteristic of many aromatic amines.

Since the hydroxyperoxy-radical is a reductant, one may expect that chain termination in an alcohol being oxidised can be caused by oxidant molecules, for example quinones. It has been shown[105] that a quinone Q inhibits the oxidation of isopropyl alcohol owing to the reactions

$$\rangle C(OH)OO^\cdot + Q \rightarrow {}^\cdot QH + \rangle C{=}O + O_2 ,$$
$$\rangle\dot{C}OH + Q \rightarrow {}^\cdot QH + \rangle C{=}O .$$

At an oxygen partial pressure of 1 atm, 86% of chain termination is due to the first reaction, the quinone being regenerated in the oxidation process.

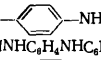
The regeneration of inhibitors in chain termination steps occurs also in the oxidation of certain unsaturated hydrocarbons, in particular 1,3-cyclohexadiene[106]. The oxidation of cyclohexadiene is propagated by hydroperoxy-radicals, which exhibit a reducing effect:



$$HO_2^\cdot + In^\cdot \rightarrow InH + O_2 .$$

The degree of regeneration of the inhibitor depends on its structure and varies over a wide range (Table 12). In the case of phenols, regeneration is observed rarely (hydroquinone); this can probably be accounted for by the very rapid recombination of PhO$^\cdot$ and $RO_2^\cdot$.

Table 12. Inhibition coefficients f for different substances undergoing oxidation.

Inhibitor	Cyclohexene (Ref.109) (60°C, O_2)	Cyclohexene + 5% cyclohexanol (Ref.109) (60°C, O_2)	Cyclohexadiene [Ref.106(75°C)]	
			O_2	in the presence of O_2
α-$C_{10}H_7NH_2$		40	28	350
α-$C_{10}H_7NHC_6H_5$	1.9	11		
β-$C_{10}H_7NH_2$	2.8	21	—	—
β-$C_{10}H_7NHC_6H_5$	1.5	35	—	—
$(C_6H_5)_2NH$	1.4	35	>200	>200
p-$NH_2C_6H_4NH_2$	2.4	28		
β-$C_{10}H_7NH$—  —NH-β-$C_{10}H_7$	2.8	130	—	—
p-$(CH_3)_2CHNHC_6H_4NHC_6H_5$	1.8	450	—	—
β-$C_{10}H_7ONH$—  —$NHO\beta$-$C_{10}H_7$	4.9	140	—	—
$(p$-$CH_3OC_6H_4)_2NH$	2.1	140	—	—
p-$(C_6H_5NH)C_6H_4NHC_6H_5$	3.5	175	—	—
			70	170
			90	1

In hydrocarbons undergoing oxidation, $f \simeq 2$ as a rule. An exception is provided by Chien's study[107], where a coefficient $f > 2$ (6–10) is quoted for 2,6-di-t-butylphenols in squalene and cyclohexene undergoing oxidation. The coefficient f was determined from the duration of the induction period in the initiated oxidation process. This measurement yields a correct value for f only if all the chains

are terminated by the inhibitor and $k_7[InH] \gg k_6[RO_2^{\cdot}]$. In the general case we have

$$W_i = k_6[RO_2^{\cdot}]^2 + fk_7[InH][RO_2^{\cdot}],\ W_{InH} = k_7[InH][RO_2^{\cdot}] \text{ and}$$

$$\frac{W_i}{W_{InH}} = f + \frac{k_6[RO_2^{\cdot}]}{k_7[InH]} = f + \frac{k_6 W_{InH}}{k_7^2[InH]^2}.$$

The coefficient f is found from the plot of w_i/w_{InH} against $w_{InH}/[InH]^2$. Such calculation based on Chien's data[107] yields $f = 2.3$ for ionol in squalene undergoing oxidation[108]. These experiments yielded an unduly high value of f because in the calculation no account was taken of chain termination by the reaction between $RO_2^{\cdot}$ radicals. Vardanyan's redetermination[108] of f for 2,6-di-t-butylphenols in cyclohexene at 80°C (in the presence of azobisisobutyronitrile as an initiator) yielded $f = 2$ for these phenols. Thus a check on Chien's results[107] failed to confirm the high values of f obtained in his study for 2,6-dialkylphenols.

XI. THE MECHANISM OF INHIBITED OXIDATION

In the absence of an inhibitor and an initiator, the mechanism of the oxidation of C–H bonds of organic compounds in the condensed phase can be represented by the following series of elementary reactions[3]:

$$RH + O_2 \rightarrow R^{\cdot} + HO_2^{\cdot}, \quad (0)$$

$$2RH + O_2 \rightarrow 2R^{\cdot} + H_2O_2, \quad (0)$$

$$R^{\cdot} + O_2 \rightarrow RO_2^{\cdot}, \quad (1)$$

$$RO_2^{\cdot} + RH \rightarrow ROOH + R^{\cdot}, \quad (2)$$

$$ROOH \rightarrow RO^{\cdot} + HO^{\cdot}, \quad (3)$$

$$ROOH \rightarrow \text{mol. products}, \quad (M)$$

$$2RO_2^{\cdot} \rightarrow \text{mol. products} \quad (6)$$

After the introduction of an inhibitor, new elementary reactions involving InH and In$^{\cdot}$ take place:

$$RO_2^{\cdot} + InH \rightarrow ROOH + In^{\cdot}, \quad (7)$$

$$In^{\cdot} + RO_2H \rightarrow InH + RO_2^{\cdot}, \quad (-7)$$

$$In^{\cdot} + RO_2^{\cdot} \rightarrow \text{mol. products} \quad (8)$$

$$In^{\cdot} + In^{\cdot} \rightarrow \text{mol. products} \quad (9)$$

$$In^{\cdot} + RH \rightarrow InH + R^{\cdot}. \quad (10)$$

As a rule, the reactions of the inhibitor with the hydroperoxide and oxygen do not play a significant role. The kinetics of inhibited oxidation can be described by a set of differential equations. Each individual substance oxidised–inhibitor system is characterised by a definite set of rate constants for reactions (0)–(10). For a comprehensive kinetic analysis of such systems, it is insufficient to base the treatment solely on experimental results. Firstly, there are very few systems in which each elementary stage has been investigated. Secondly, in the experiment it is always possible that a number of factors (and elementary reactions) have not been taken into account. There is a possibility that the presence of substances (impurities) may complicate the mechanism, etc. Therefore, in a study of complex reactions such as the inhibited oxidation processes, the experimental research techniques can be usefully supplemented by the so called numerical experiment where the mechanism is specified in the form of a set of differential equations and rate constants and a computer calculation yields the rates of accumulation of reaction products. The numerical experiment yields the reaction kinetics for strictly specified mechanism and constants; the element of uncertainty associated with incomplete control over the reaction mechanism in a real experiment is excluded here; the reaction mechanism can be varied at will, which makes it possible to establish clearly the role of a particular elementary reaction in the overall process. Such a calculation has been carried out[110] for the simplest case where the inhibitor is involved only in reaction (7) and In$^{\cdot}$ is involved only in reaction (8). A more complicated mechanism, including reactions (7)–(10) was examined with the following rate constants: $W = \{k_0 + k_0'[RH]\}[RH][O_2] = 10^{-10}$ mole litre^{-1} s^{-1}, $k_2[RH] = 50$ s^{-1}, $k_3 = 2 \times 10^{-6}$ s^{-1}, $k_M = 5 \times 10^{-5}$ s^{-1}, $k_6 = 10^6$ litre mole^{-1}s^{-1}, $k_7 = 2 \times 10^5$ litre mole^{-1}s^{-1}, $k_{-7} = 10^5$ litre mole^{-1}s^{-1}, $k_8 = 10^9$ litre mole^{-1}s^{-1}, $k_9 = 10^8$ litre mole^{-1}s^{-1}, and $k_{10} = 10$ litre mole^{-1}s^{-1}. To elucidate the role of each of these reactions involving In$^{\cdot}$, a numerical experiment was carried out including the mechanism of individual (but not all) reactions of the In$^{\cdot}$ radical.

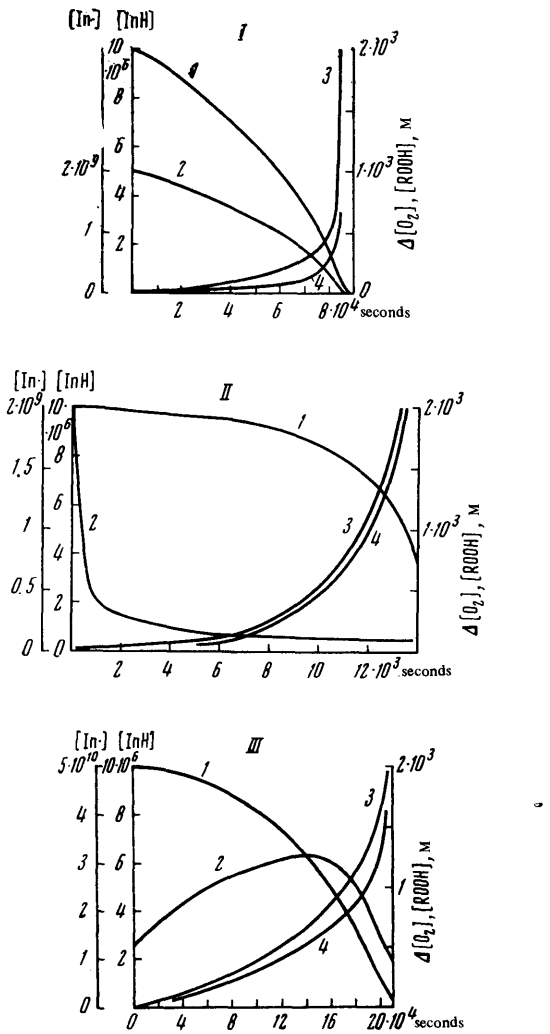


Figure 2. Kinetic curves for the consumption of InH (curve *1*) and In$^{\cdot}$ (curve *2*), the absorption of O_2 (curve *3*) and the accumulation of ROOH (curve *4*) in mechanisms I, II, and III respectively.

Mechanism I: the inhibitor and the radical In$^{\cdot}$ react with $RO_2^{\cdot}$, the rate constants for the remaining reactions of In$^{\cdot}$ being zero. In this case the oxidation develops very slowly and the transition from slow inhibited oxidation to rapid oxidation takes place abruptly (Fig. 2, I). The concentration of In$^{\cdot}$ varies in parallel with [InH]. At the end of the induction period, the concentration of ROOH is less than that of the absorbed oxygen.

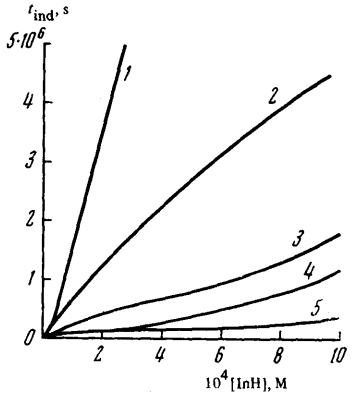


Figure 3. Dependence on the induction period on the concentration of inhibitor: 1) mechanism I; 2) mechanism III + Q with $k_Q = 1$; 3) mechanism III + Q with $k_Q = 0.2$; 4) mechanism III + Q with $k_Q = 0.02$; 5) mechanism II; Q = inhibitor decomposing the hydroperoxide; $[Q]_0 = 10^{-3}$ M.

Mechanism II: the radical In$^{\cdot}$ reacts only with $RO_2^{\cdot}$ and ROOH. Fig. 2, II shows that the oxidation develops more rapidly than in mechanism I, the proportion of the hydroperoxide decomposing during the induction period is small, and the concentration of In$^{\cdot}$ decreases rapidly during the reaction. The reaction emerges from the induction period smoothly long before the complete consumption of the inhibitor.

Mechanism III: the radical In$^{\cdot}$ reacts with $RO_2^{\cdot}$, In$^{\cdot}$, and RH. The oxidation develops faster than in mechanism I; the reaction emerges from the induction period smoothly, the concentration of In$^{\cdot}$ passing through a maximum (Fig. 2, III). Comparison of mechanisms (I)–(III) (Fig. 2) shows that a change in mechanism causes a significant change in the kinetics of the accumulation of In$^{\cdot}$. There is also a change in the nature of the relation between the induction period and [InH] (Fig. 3). For mechanism I, the relation is close to linear. When In$^{\cdot}$ causes chain propagation via the reaction with RH, the induction period ceases to depend on [InH] beyond a certain value $[InH]_{min}$. For mechanism II, the relation between t_{ind} and [InH] is represented by a line with positive curvature. In the presence of an additional inhibitor Q decomposing the hydroperoxide, the t_{ind}–[InH] relation is represented by an inverted S-shaped curve (Fig. 3). Evidently different mechanisms of inhibitor action lead to different relations between t_{ind} and [InH]. However, one should bear in mind that the mechanism of inhibitor action cannot be inferred unambiguously from the t_{ind}–[InH] relation.

XII. CRITERIA OF THE EFFICIENCY OF INHIBITORS

We have seen that the mechanism of the action of inhibitors is fairly complicated. The efficiency of the inhibiting effect depends on a series of reactions involving In$^{\cdot}$, $RO_2^{\cdot}$, InH, and ROOH, i.e. is determined by a series of reactions. Therefore the efficiency of the inhibitor cannot be expressed by any one parameter but must be represented in the general case by a set of formulae (inequalities), which take account of the contributions by all the reactions on which the rate of the oxidation process depends.

If the radicals In$^{\cdot}$ are only weakly involved in chain propagation,

$$k_6[RO_2^{\cdot}] \gg k_{10}[RH] + k_7[ROOH] \quad \text{or}$$
$$k_6 W_i / f k_7 [InH] \gg k_{10}[RH] + k_{-7}[ROOH],$$

the inhibiting effect is stronger for higher values of k_7 and [InH]:

$$f k_7 [InH][RO_2^{\cdot}] \gg k_6 [RO_2^{\cdot}]^2 \text{ and } f k_7 [InH] \gg \sqrt{W_i k_6} \quad \text{(IV)}$$

If In$^{\cdot}$ is involved in chain propagation via reaction (10), then strong inhibition requires that the following inequality should hold:

$$k_2[RH][RO_2^{\cdot}] + k_{10}[RH][In^{\cdot}] \ll k_2[RH]\sqrt{W_i/k_6} \quad \text{or}$$
$$1 + \frac{k_7[InH]}{k_2[RH]} \ll k_2 \left\{ \frac{2k_8}{k_6} \frac{k_7[InH]}{k_{10}[RH]} + \frac{2k_9}{k_6} \left(\frac{k_7[InH]}{k_{10}[RH]} \right)^2 \right\}^{1/2}.$$

The above inequality is valid when another inequality holds:

$$\frac{1}{k_{10}} \gg \frac{k_6[RH]}{8k_2^2 k_8} \left(1 + \frac{1}{k_7[InH]} \right) + \frac{\sqrt{k_6}}{4k_2\sqrt{2k_9}} \left(\frac{1}{k_2} + \frac{[RH]}{k_7[InH]} \right), \quad \text{(V)}$$

i.e. when k_{10} is fairly large, it is impossible to achieve effective inhibition by increasing [InH] if

$$\frac{1}{k_{10}} \lesssim \frac{k_6[RH]}{8k_2^2 k_8} + \frac{\sqrt{k_6}}{4k_2^2\sqrt{2k_9}}.$$

If In$^{\cdot}$ causes chain propagation via the reaction with the hydroperoxide, we obtain the following inequality for effective inhibition:

$$[RO_2^{\cdot}] \ll \sqrt{W_i/k_6}, \quad [RO_2^{\cdot}] = \left\{ \frac{W_i k_{-7}[ROOH]}{2k_7 k_8 [InH]} \right\}^{1/2}$$

and

$$k_{-7} \ll \frac{2k_7 k_8 [InH]}{k_6 [ROOH]} \quad \text{(VI)}$$

In certain cases one should also bear in mind the reaction of the inhibitor itself with the hydroperoxide:

$$ROOH + InH \rightarrow RO^{\cdot} + H_2O + In^{\cdot} \quad (11)$$

When account is taken of this reaction in the presence of InH, $W_i = W_0 + 2k_3[ROOH] + 2ek_{11}[ROOH][InH]$. If we consider the case where In$^{\cdot}$ is responsible for chain propagation only via the reaction with the hydroperoxide, then, when account is taken of reaction (11), we obtain the following inequality for effective inhibition:

$$\frac{k_{-7}[ROOH](1 + ek_{11}[InH]/k_3)}{2k_7 k_8} \ll \frac{1}{k_6} \quad \text{or}$$
$$\frac{k_{-7}}{[InH]} + \frac{ek_{-7}k_{11}}{k_3} \ll \frac{2k_7 k_8}{k_6 [ROOH]}. \quad \text{(VII)}$$

Inequalities (IV)–(VII) represent a combined kinetic criterion for an effective inhibitor in the given compound being oxidised. These inequalities take into account all the reactions involving the inhibitor currently known.

They reflect both the specific characteristics of the inhibitor, its kinetic features (the constants k_7, k_{-7}, k_8, k_9, k_{10}, and k_{11}), and the specific features of the substance being oxidised (W_0, k_2, and k_{10}), its peroxy-radicals (k_2, k_6, k_7, and k_8), and its hydroperoxide (k_3, k_{-7}, and k_{11}).

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The review shows that the principal reactions involved in oxidation inhibited by phenols and aromatic amines have now been established. The rate constants for reactions with peroxy-radicals have been measured for many phenols and aromatic amines. Unfortunately in the vast majority of cases these measurements have been made at only one temperature, which makes it difficult to employ the results at other temperatures. The reactions of phenoxy- and phenylnitrogen radicals have been less well investigated, particularly in the case of the reactive radicals In$^{\cdot}$, such reactions playing a major role in inhibited oxidation. There are few data for the rates of the reactions between In$^{\cdot}$ and $RO_2^{\cdot}$ and between In$^{\cdot}$ radicals alone. Overall, a quantitative study of the mechanism of the action of inhibitors requires further research to establish from the available fragmentary data a well-founded mechanism of inhibitor action.

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Institute of Chemical Physics,
USSR Academy of Sciences,
Moscow

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Kinetics of the Photochemical Oxidation of Polyolefins

O.N.Karpukhin and E.M.Slobodetskaya

The review gives a general and systematic account of data on the kinetics of the thermal and photochemical oxidation of polyolefins and the kinetic parameters obtained by different investigators are compared. The kinetic parameters found at different temperatures and extrapolated to natural conditions are quoted and kinetic curves for the photochemical oxidation of polyolefins are calculated. The curves agree satisfactorily with experimental data on the accumulation of polyolefin photochemical oxidation products.
The bibliography includes 104 references.

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I. INTRODUCTION

Polyolefins are polymers which consist of weakly branched hydrocarbon molecules. The most common and industrially most important examples of this series of polymers are polyethylene (PE) and polypropylene (PP).

On ageing, the mechanical properties of articles made of these polymers are impaired, they become brittle, yellow-coloured, and covered in cracks, their tensile strength falls, etc. The main cause of these changes is oxidative degradation of the polymer[1].

According to modern ideas, the oxidation of polymers is a degenerate branched radical chain process, the principal stages of which are initiation of the oxidation chains, their propagation and termination, the formation of a degenerate-branching agent, and degenerate-branching of the chains by this species. The characteristic features of the mechanisms of each of these stages at high temperatures (120—150°C) have been fairly well investigated. The branching agent is a peroxide formed in the chain propagation step. In air, alkyl radicals are largely converted into peroxy-radicals, which are responsible for the propagation of the oxidation chain. Chain termination occurs in the peroxy-radical disproportionation step with formation of alcohols and carbonyl compounds. The polymeric molecule is ruptured in the chain propagation stage, during the decomposition of the peroxy-radicals, and possibly in the branching stage during the decomposition of the hydroperoxide[2]. In the case of a pure polyolefin, the overall process is satisfactorily interpreted as a degenerate-branched chain reaction with quadratic destruction of active centres[2].

When polymers are used close to room temperature, the rate of chain branching due to the thermal decomposition of the peroxide becomes low due to the high activation energy for this reaction (about 30 kcal mole^{-1}). Under these conditions, the photochemical reactions in the polymer begin to play an important role. The oxidation products of polyolefins absorb light much more effectively than the initial polymeric molecule. Therefore one may expect that the photochemical oxidation of polyolefins is also a degenerate branched chain process in which the initiation and chain branching steps involve light quanta.

At the beginning of the present review, each stage of the process is considered separately and then the results of the treatment are compared with the macroscopic relations observed experimentally.

II. SENSITISED PHOTOCHEMICAL OXIDATION OF POLYOLEFINS

A saturated hydrocarbon molecule of any length and with any degree of branching does not absorb light at wavelengths above 200 nm, i.e. does not absorb sunlight reaching the surface of the earth. Fig. 1 presents the absorption spectrum of saturated hydrocarbons and the spectral composition of sunlight on the earth's surface† and at the limit of the atmosphere. It shows that the spectra hardly overlap, i.e. pure olefins should not be decomposed by sunlight and the reason for their chemical degradation must be some light-absorbing impurities.

Probably all the impurities present in polymers can be divided into two groups. Firstly, these are extraneous impurities which enter the polymer in some way: the residues from the catalyst, impurities sorbed by the polymer in the course of its manufacture and use, special additives to polyolefins, fillers, thermostabilisers, etc. Secondly, these are polymer reaction products: peroxides, carbonyl compounds, olefinic compounds, etc. Impurities of the first type can initiate the photochemical oxidation of the polymer, while those of the second type are responsible for degenerate chain branching during photochemical oxidation.

Fig. 2 presents the absorption spectra of the main impurities usually detected in polyolefins. They all absorb light at longer wavelengths much more effectively than polyolefins. Many of these impurities are photochemically active. For example, thermostabilisers

† The spectrum of sunlight in space in the earth's orbit was taken from Ref. 4 and the emission spectrum of the sun in the upper layers of the atmosphere and for different positions of the sun above the horizon was calculated from the absorption spectrum of ozone, which absorbs the ultraviolet component of the sun's spectrum.

usually contain phenols or aromatic amines. Compounds of both classes are known to be effective photosensitisers[3]. Attention has been drawn[3] to the fact that the photochemical degradation of polyolefins is much faster in the presence of aromatic hydrocarbons sorbed from air. Fig. 2 shows that the extinction coefficients of these substances are very large and their photosensitising activity is also well known.

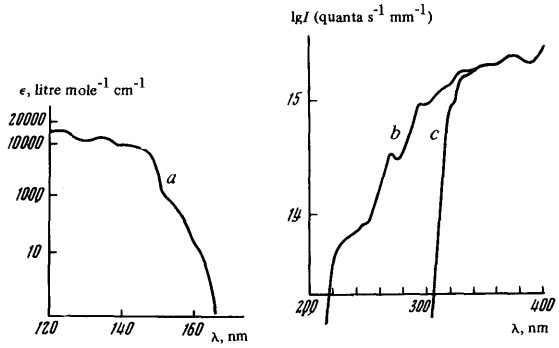


Figure 1. Absorption spectrum of n-butane (*a*) and the spectral composition of sunlight at the limit of the atmosphere (*b*) and on the surface of the earth (*c*).

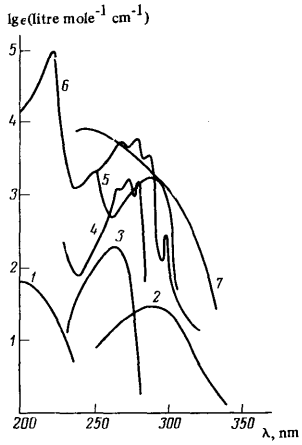
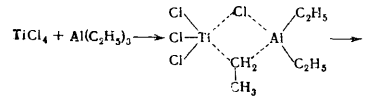


Figure 2. Absorption spectra of the main impurities in polyolefins: 1) acetic acid; 2) aliphatic ketones; 3) benzene; 4) phenol; 5) aniline; 6) naphthalene; 7) $Ti(OC_4H_9)_4$.

In a number of studies, it has been asserted that the main cause of the photochemical degradation of polymers is the presence of residues from the catalyst in the polymer. However, the photochemical activity of these compounds has not yet been investigated in detail. Moreover it is difficult to specify an individual substance responsible for their photochemical activity[4,5]. One can only point to studies where it has been shown that the presence of the catalyst at a low concentration accelerates the photochemical degradation of the polymer[5-8].

Ziegler—Natta catalysts, which are nowadays most widely employed, consist of a mixture of compounds of variable-valence metals (titanium, chromium, molybdenum, vanadium, etc.) and organometallic compounds, mainly aluminium derivatives. The principle of their action can be illustrated by the following scheme[9]:



$$\longrightarrow (C_2H_5)_2AlCl + Cl_3Ti{\cdots}C_2H_5 \longrightarrow TiCl_3 + C_2H_5^{\cdot}$$

Catalysts are removed from polymers by washing them with alcohols (isopropyl, butyl, etc. alcohols) but part of the catalyst nevertheless remains in the polymer. According to the data of Balabau and Preisler[10], less than 0.005% (0.001 M) of titanium and aluminium derivatives remains in polypropylene purified in this way. The residual catalyst has a fairly high extinction coefficient at about 300 nm (Fig. 2). The absorption of a light quantum may result in the formation of free radicals by the reaction[6]

$$M^{n+}X^{\cdot} + h\nu \rightarrow M^{+(n-1)} + X^{\cdot}$$

The occurrence of this reaction is postulated[6] by analogy with the corresponding reactions in a liquid, usually aqueous solution[11]. Neither the quantum yield of reactions of this kind nor details of the mechanism have been investigated.

The concentration of impurities in the polymer is of the order of 10^{-2}—10^{-3} M, i.e. it corresponds approximately to the concentration in the polymer of macromolecules with a molecular weight of 10^5—10^6. Thus if the impurities were decomposed in the photosensitisation step, the molecular weight of the polymer would decrease at most by a factor of several units and polymer degradation would then stop. The rate of the degradation process would then decrease with time. In fact, according to the literature, the accumulation of carbonyl groups, for example in the photochemical oxidation of polypropylene[12-14], is autocatalytic and the initial rate of these processes is very low. When the residual catalyst is introduced at a concentration up to 0.03 M (Ti), the photochemical reaction remains autocatalytic[10].

The data quoted show that impurities can have a significant influence only in the initial stage of the process, while at advanced stages of the latter impurities of the second kind, i.e. products formed in the course of the degradation of the polymer, play the main role.

III. DEGENERATE CHAIN BRANCHING IN THE PHOTOCHEMICAL OXIDATION REACTION (PHOTOLYSIS OF THE POLYOLEFIN OXIDATION PRODUCTS)

As mentioned above, degenerate chain branching in the photochemical oxidation of polyolefins can involve hydroperoxides and ketones. For a better understanding of this stage of the process, we shall consider the photolysis of these compounds.

1. Photochemistry of Aliphatic Ketones

The mechanism of the photolysis of low-molecular-weight aliphatic ketones has been investigated very intensively and is now believed to be largely understood.

Aliphatic ketones have an absorption maximum in the range 270—290 nm, their absorption bands extending up to 320—330 nm (for example the molar extinction coefficient of diethyl ketone is $\epsilon_{313} = 2.07$). This absorption is due to a forbidden singlet—singlet transition with electron transfer from the non-bonding n orbital located on the oxygen atom to the more delocalised π^* orbital of the carbonyl group. The same transition probably occurs in a polymer containing keto-groups. For example, the maximum in the absorption spectrum of the ethylene—carbon monoxide copolymer (1% CO), which has the same physical properties as low-pressure polyethylene, is very close to the absorption maximum of an aliphatic ketone[15] (Fig. 3).

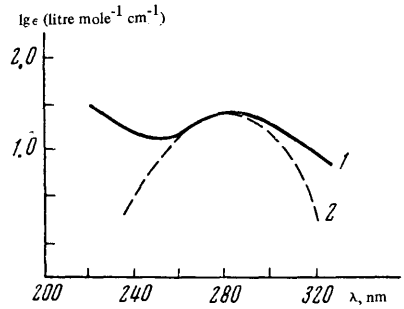


Figure 3. Absorption spectra of the ethylene—carbon monoxide (1%) copolymer (curve *1*) and of the ketone $CH_3(CH_2)_{10}CO(CH_2)_{10}CH_3$ (curve *2*) in heptane at 80°C.

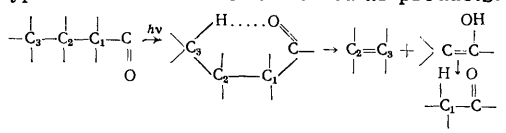
A very short time after the absorption of a light quantum, of the order of 10^{-11} s in the condensed phase, the excited electronic singlet state $^1(n, \pi^*)$ of carbonyl compounds is thermally equilibrated with the medium, whence the molecules can pass to the triplet state $^3(n, \pi^*)$ or can dissipate the excess energy in the form of heat.

Carbonyl compounds in the singlet and triplet excited states can also enter into chemical decomposition, addition, isomerisation, etc. reactions.

Numerous studies on the photolysis of ketones have shown that there are two main pathways to their decomposition, which are referred to in the literature as the Norrish type I and II reactions. The decomposition of ketones via the type I reaction results in the formation of free radicals:

$$R_1—\underset{\underset{O}{\|}}{C}—R_2 \xrightarrow{h\nu} R_1—\underset{\underset{O}{\|}}{C}\cdot + R_2^{\cdot} \quad \text{or} \quad R_1^{\cdot} + R_2^{\cdot} + CO$$

which can then react with the solvent. The decomposition via the type II reaction leads to molecular products:



Since decomposition via the type II reaction requires the formation of an intermediate six-membered complex, only ketones with at least one hydrogen atom in the γ-position relative to the carbonyl group can decompose via this pathway, i.e. in polyolefins with C=O groups in the main chain there is a possibility of an intramolecular hydrogen transfer in which an olefin and an enol are formed, the latter in its turn giving rise to a ketone with a shorter chain.

Hartley and Guillet[16] investigated the photolysis of model aliphatic ketones R—C(O)—R, with the chain length of the alkyl group ranging from C_7 to C_{43}, under the influence of light at a wavelength of 313 nm. It was shown that the decomposition quantum yields φ_I and φ_{II} depend on the chain length of the alkyl group in the ketone, viscosity, and temperature. Fig. 4 shows the variation of φ_I and φ_{II} with the chain length of the alkyl group. It is seen that an increase in the length of the carbon atom chain entails a decrease of φ_I and φ_{II}, φ_I reaching a limiting value at C_{40} and φ_{II} falling rapidly with increase of chain length and reaching 0.06 for the ketone containing 43 carbon atoms. After this, φ_{II} decreases much more slowly reaching a value of 0.025 in the polyethylene copolymer containing 1% CO.

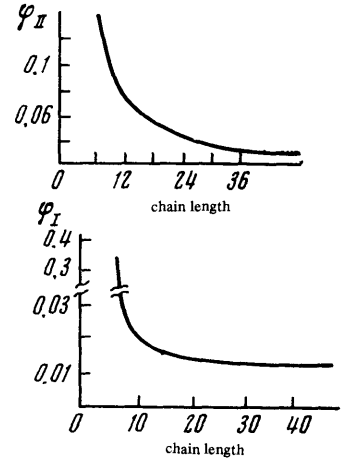


Figure 4. Variation of the quantum yields φ_I and φ_{II} of the decomposition of ketones with the length of the chain of the alkyl group (in liquid paraffin at 70°C).

The decrease of the quantum yield is probably caused by an increase in the probability of radiationless dissipation of energy with increase of the number of atoms in the ketone molecule. Table 1 presents the temperature variation of the quantum yields for the formation of the photochemical decomposition products of pentadecan-8-one, which decomposes according to the mechanism

$$CH_3(CH_2)_5CO(CH_2)_6CH_3 \xrightarrow[II]{h\nu} CH_2{=}CH(CH_2)_3CH_3 + CH_3CO(CH_2)_6CH_3,$$

$$CH_3(CH_2)_5CO(CH_2)_6CH_3 \xrightarrow[I]{h\nu} CH_3(CH_2)_6\cdot + \cdot CO(CH_2)_6CH_3$$

$$CH_3(CH_2)_6\cdot + CO.$$

The data in Table 1 show that the quantum yield of the type II reaction does not depend appreciably on temperature ($E_{act} \simeq 1$ kcal mole^{-1}). On the other hand, the quantum yield in the formation of heptane via the type I reaction increases fairly rapidly with temperature ($E_{act} = 4.8$ kcal mole^{-1}). The results can be explained bearing in mind that the type I reaction involves the dissociation of a bond in the molecule with formation of radicals. Consequently it should depend on temperature, albeit not as

markedly as the analogous thermal bond dissociation. An essential requirement for the type II reaction is the formation of a six-membered complex, which depends only on the extent to which the internal rotation of the groups in the molecule is free and this in turn is independent of temperature above the glass point of the polymer. φ_I and φ_{II} were found to be virtually independent of viscosity, which was varied from 0.28 to 9.2 cP.

Table 1.

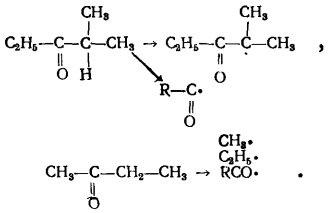
T, °C	$\varphi_I \times 10^4$	φ_{II}	φ_{II}
	heptane	hex-1-ene	nonan-2-one
30	0.22	0.066	0.067
60	0.42	0.068	0.067
90	0.87	0.091	0.086
120	1.4	0.087	0.091
145	1.9	0.092	0,102

Table 2.

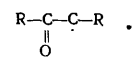
T, °C	Quantum yield of rupture reactions $\varphi_I + \varphi_{II}$	Quantum yield for accumulation of vinyl groups	
		φ_{II}	φ_I
120	0.05	0.025	0.025
90	0.04	0.025	0.015
25	0.028	0.025	0.003
—25	—	0.025	—
—50	—	0.020	—
—68	—	0.013	—
—95	—	0.005	—
—150	—	0.000	—

Both singlet and triplet states are involved in the photolysis of aliphatic ketones. Thus the photochemical decomposition of undecan-6-one is inhibited by cyclooctadiene (COD), a triplet acceptor, to an extent not greater than 55%;[17] similar results were obtained for certain other ketones and acceptors in studies[18-23] where it was shown that approximately 60—90% of the reactions in the photolysis of aliphatic ketones involve triplet levels. These results suggest that an appreciable proportion of the ketones decompose with participation of triplet states, but the mechanism of the decomposition, which is not inhibited by triplet acceptors, remains obscure.

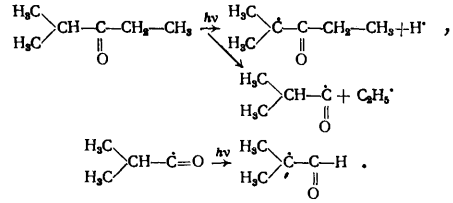
At low temperatures (77°K) the photochemical decomposition of aliphatic ketones (at wavelengths from 260 to 360 nm) leads to the formation of radicals at an appreciable concentration[24]. For example, the photolysis of ethyl isopropyl and ethyl methyl ketones results in the formation of radicals via the reactions



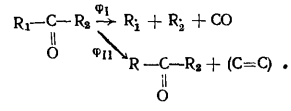
When specimens are irradiated with light at a wavelength higher than 400 nm and heated to −140°C, the singlet line of the R—Ċ=O radicals in the ESR spectrum disappears and only radicals in which the C=O group and the unpaired electron are separated remain:



On the basis of these data, the following mechanism has been proposed[24] for the photolysis of aliphatic ketones with dissociation of the C—C bonds adjoining the carbonyl group:



Thus analysis of data for the photolysis of low-molecular-weight aliphatic ketones made it possible to predict certain photochemical properties of polymeric ketones. The $R_1-\underset{\underset{O}{\|}}{C}-R_2$ polymeric ketone should probably decompose via type I and II Norrish reactions like aliphatic ketones:

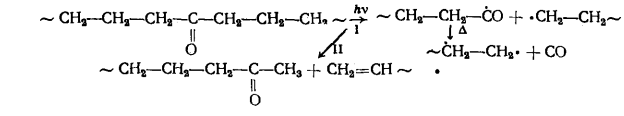


All polymeric ketones should decompose at room temperature via the type I reaction with a quantum yield of 0.05—0.1. Only ketones capable of forming the necessary six-membered complex, i.e. having a hydrogen atom joined to the carbon atom in the γ-position relative to the C=O group, decompose via the type II reaction.

On reducing the temperature, the quantum yield of the type I reaction changes slowly and the activation energy is 5 kcal mole^{-1}. The type II reaction depends significantly less on temperature but its contribution diminishes sharply with increase of the length of the R_1 and R_2 groups. Its importance can be appreciable only above the glass point of the polymer, since at lower temperatures the free rotation of the groups in the units of the macromolecule is inhibited, or in the decomposition of ketones with a C=O group close to the end of the polymer chain when at least one of the radicals formed is small.

The breaks in the polymer molecule lead to a significant change of the molecular weight of the polymer in both reactions only when the recombination of radicals formed in the type I reaction is ruled out. These conclusions have been confirmed quantitatively by the results of studies on the photolysis of pre-oxidised polypropylene and of the ethylene—carbon monoxide copolymer[15].

The physical properties of the ethylene—carbon monoxide copolymer containing 1—9% of carbon monoxide are the same as those of a low-pressure polyethylene. The polymer was irradiated with monochromatic light at a wavelength of 313 nm in decalin solution, and a decrease of its molecular weight, evolution of carbon monoxide, and the formation of vinyl groups were observed. These results were accounted for by the following reactions in the polymer:

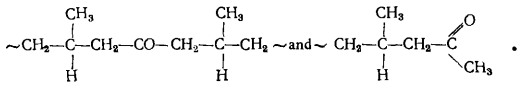


Carbon monoxide and polymeric radicals are formed by the type I reaction and the type II reaction gives rise to terminal ketones and vinyl groups. Polymer chains are ruptured in both reactions. In solution the polymeric radicals abstract a hydrogen atom from the solvent molecule and do not recombine with one another, so that the quantum yield of the rupture reactions is equal to the sum of the quantum yields of both reactions. The quantum yield of the type II reaction was determined from the change in the concentration of vinyl groups. Table 2 presents the relation between the quantum yields of both reactions and temperature.

Table 2 shows that the quantum yields of the type I reaction becomes significant above 25°C, where the quantum yield of the type II reaction is independent of temperature. This can be explained as follows. It has been established[25,26] that at −30°C free rotation about the C—C bond in polyethylene is hindered and hindered joint rotation of at least three units arises. At −120°C, the joint rotation is also inhibited. Since the properties of the copolymer are similar to those of low-pressure polyethylene, retardation of free rotation about the C—C bond can also be expected near −30°C, the probability of the formation of a six-membered complex and hence φ_{II} diminishing. At −120°C, φ_{II} becomes zero. Above −30°C, where rotation is not hindered, φ_{II} should be independent of temperature, which is in fact observed experimentally.

In the solid polymer the quantum yield of the formation of vinyl groups at 25° and 90°C does not differ from φ_{II} in solution[15]. This can be explained by the fact that the destruction of radicals formed in the type I reaction does not involve the formation of double bonds (the radicals do not disproportionate but recombine). Therefore in this case the quantum yield of the rupture reactions is probably determined by φ_{II}. Unfortunately Hartley and Guillet[15] did not make such measurements. The type I and II reactions probably also occur in the photolysis of poly(methyl vinyl ketone) containing the C=O group in the side chain[27]. The quantum yield of the type I reaction, determined from the evolution of carbon monoxide and methane, increases with temperature, as for the copolymer (25—80°C), and the occurrence of the type II reaction was established on the basis of the increase of the optical density in the range 220—230 nm, which was attributed to the accumulation of double bonds.

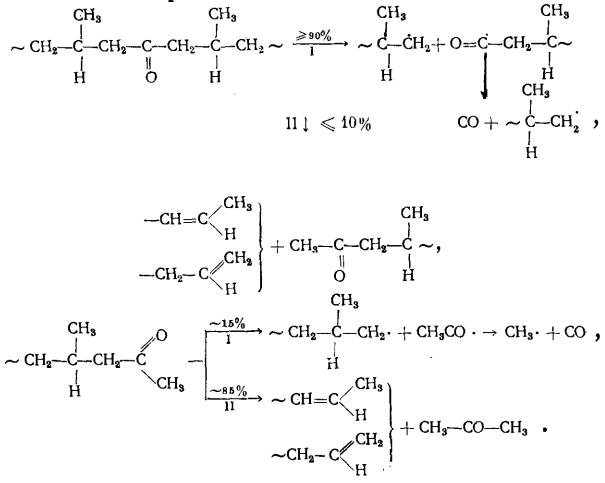
It has been shown[17] that at 80°C the triplet quenching agent COD retards the photochemical degradation of the ethylene—carbon monoxide copolymer in solution and the accumulation of vinyl groups in the solid phase by a factor not greater than two. In contrast to the ethylene—carbon monoxide copolymer, where the carbonyl groups were distributed only in the centre of the polymer chain, preoxidised (225°C) polypropylene contains two main types of keto-groups[28]:



(A) (B)

In the photolysis of oxidised polypropylene containing type (A) and (B) keto-groups, a decrease in the weight of the polymer was observed and the composition of the volatile products and the change of the optical density at the absorption maxima of the fragments (A) and (B) (1718 and 1726 cm^{-1} respectively) were analysed. The quantum yields for the decomposition of both ketones were approximately identical, amounting to 0.07 and 0.08 respectively.

Analysis of the volatile products (CH_4, CO, CO_2, C_2H_6, etc.) led to the conclusion that the ketones A and B decompose via the Norrish type I and II reactions, the ketone (A) decomposing mainly into radicals and the ketone (B) into molecular products:



This set of reactions provides a satisfactory description also of the kinetics of weight loss by the polymer.

Despite the fact that the photolysis of ketones involves the rupture of the chain, an appreciable decrease of viscosity on irradiation was not observed[28]:

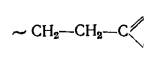
η before irradiation = 0.63; $M_v = 5.2 \times 10^4$,

η after irradiation = 0.60; $M_v = 4.8 \times 10^4$.

The present authors' calculation of the quantum yield of the rupture reactions on the basis of these data is 4×10^{-3}, which is consistent with the fact that the chain is ruptured only on decomposition of the central ketone (A) via the type II reaction. The macroradicals formed from the ketone (A) via the type I reaction and following the abstraction of a hydrogen atom from the macromolecule by the methyl radical [formed from the ketone (B) via the type I reaction] probably recombine, which does not lead to a decrease of the molecular weight of the polymer.

As was to be expected, the quantum yield for the decomposition of the terminal ketone via the type II reaction is higher by a power of ten, since the mass of one of the radicals adjoining the carbonyl group is small. The quantum yield of the type (I) reaction determined by Carlsson and Wiles[28] also exceeds the quantum yield of this reaction in the ethylene—carbon monoxide copolymer. We believe this to indicate that the rupture of the copolymer in the type II reaction takes place closer to the end of the molecule; owing to a change in the molecular weight distribution, the quantum yield of the rupture reactions found by Hartley and Guillet[15] from the change in viscosity is not equal to the sum of the quantum yields of the type I and II reactions and the values of $\varphi_I + \varphi_{II}$ and φ_I quoted in Table 2 are significantly too low.

We explain the change in molecular weight observed during the photolysis of the ethylene—carbon monoxide copolymer in decalin by the fact that the macroradicals formed abstract a hydrogen atom from the solvent, which results in the formation of a macromolecule with a lower molecular weight. We have been unable to find any studies on the photolysis of preoxidised polyethylene, but, if the latter contains terminal ketones,



their decomposition via the type I reaction should lead to the formation of low-molecular-weight CH_3 radicals. The recombination of these radicals with the polymer macroradicals gives rise to molecules with a lower molecular weight and the quantum yield of the rupture reactions should be relatively high, since the probability that the methyl radical abstracts a secondary hydrogen atom from polyethylene is lower than the probability that it abstracts a tertiary hydrogen atom from polypropylene.

2. Photolysis of Hydroperoxides and Peroxides

The decomposition of dialkyl peroxides (dimethyl peroxide[29], diethyl peroxide[30,31], ethyl t-pentyl peroxide[29], di-isopropyl peroxide[32,33], t-butyl isopropyl peroxide[29], and di-t-butyl peroxide[34-40]) in the gas phase has been investigated most thoroughly. It has been established that even in the gas phase the absorption spectra of these peroxides do not exhibit any structure (Fig. 5). This suggests that the O—O bond is dissociated immediately on absorption of a light quantum, without proceeding via an intermediate excited state, and two free radicals are formed.

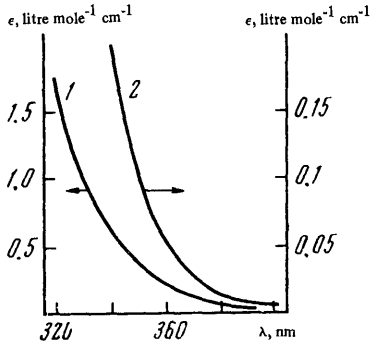


Figure 5. Absorption spectra of di-t-butyl peroxide (curve *1*) and t-butyl hydroperoxide (curve *2*).

The energy of the O—O bond in peroxides is less than 40 kcal mole^{-1}. Consequently, on irradiation with light at a wavelength of 254 nm, the excess energy of about 70 kcal mole^{-1} is distributed between two radicals. Therefore the absorption of each light quantum leads not only to the dissociation of the O—O bond but also to the formation of so called hot radicals carrying the excess energy.

The presence of a large energy excess in the radicals formed is confirmed by the analysis of the products of the photolytic decomposition of peroxides. Hot radicals readily decompose until they attain thermal equilibrium. For example, in the photolysis of di-t-butyl peroxide, acetone, methane, and ethane were detected in addition to other products; these can be accounted for by the following reactions:

$$(CH_3)_3CO^{\cdot *} \rightarrow CH_3^{\cdot} + CH_3COCH_3,$$

$$CH_3^{\cdot} + CH_3^{\cdot} \rightarrow C_2H_6 \text{ etc.}$$

McMillan[32], who investigated the photolysis of peroxides in the presence of nitric oxide (NO) as an inhibitor, reached the same conclusion. Apart from nitrites and nitrates, other products, mainly acetone, were detected in the peroxide decomposition products. On the hypothesis that only "non-hot" radicals react with the inhibitor and "hot" radicals decompose during this period, the fraction α of "hot" radicals formed in the photolysis of peroxides was determined. For example, $\alpha_{313} = 0.21$ and $\alpha_{254} = 0.6$ for di-isopropyl peroxide.

The characteristics of the photolysis of peroxides and hydroperoxides in solutions are largely the same as those of their decomposition in the gas phase. As in the gas phase, they decompose into radicals, probably without proceeding via an intermediate excited state. The absence of any long-lived excited state of the peroxide in the condensed phase is suggested to some extent by the finding that no investigation showed a retardation of their photochemical decomposition by any excited state quenching agents.

Nevertheless, the dependence of the composition of the photochemical decomposition products on the wavelength of the exciting light (Table 3) indicates the existence of hot species or complex pathways in the decomposition of peroxides by light of shorter wavelengths. The primary radical formed in the decomposition of dicumenyl peroxide (DCP) can decompose into acetone and a phenyl radical or into acetophenone and a methyl radical. This decomposition can occur in the primary photochemical step

$$[C_6H_5(CH_3)_2CO]_2 + h\nu \rightarrow \begin{cases} C_6H_5C(CH_3)_2O^{\cdot} + CH_3COCH_3 + C_6H_5^{\cdot} \\ 2C_6H_5(CH_3)_2CO^{\cdot} + 2CH_3^{\cdot} \text{ etc.} \end{cases}$$

Table 3. Yield of the main products of the decomposition of DCP at 20°C [42] as a percentage of the peroxide decomposed.

Decomposition product	Solvent			
	n-hexane		CCl_4	
	wavelength, nm			
	313	254	313	254
Dimethylbenzyl alcohol	95—100	90—95	—	—
Acetophenone	2	4	95—100	30
Acetone	—	—	5	70

The principal distinctive feature of the photochemical decomposition of peroxides in the condensed phase is a significant influence of the solvent on the composition of the decomposition products and the occurrence of induced decomposition of peroxides. For example, a study has been made[41,42] of the decomposition of t-butylhydroperoxide (TBHP) and DCP in n-hexane and carbon tetrachoride. Tables 3 and 4 present the compositions of the photolysis products of these peroxides.

The authors explain the observed composition of the products by the fact that, in solvents capable of hydrogenating the radicals (n-hexane), an alcohol may be formed by the reaction between the alkoxy-radical and the solvent. The occurrence of these reactions leads to an increase in the quantum yield of the photolysis of the peroxide owing to the induced radical decomposition. For example, the quantum yield of the decomposition of TBHP is 3.9 in n-heptane and 1.57 in DCP.

According to Martin and Norrish[41], in a solvent incapable of hydrogenating the radicals (carbon tetrachloride) the induced decomposition of the peroxide is due to the radicals formed from it.

Table 4. Main decomposition products of TBHP at 20°C [41] at 313 nm.

Decomposition products in CCl_4	Yield, % of decomposed peroxide	Decomposition products in n-hexane	Yield, % of decomposed peroxide
Oxygen	41.7	Oxygen	7.1
Carbon monoxide	0.72		
Carbon dioxide	—	Formic acid	1.2
t-Butyl alcohol	97	Alcohol	156
Acetone	3.1	Acetone	8.3
Water	5.4	Water	21

The validity of the above mechanisms for the decomposition of peroxy-compounds is confirmed by ESR data. Despite numerous attempts by various investigators, alkoxy-radicals were not detected in the photolysis of peroxides and hydroperoxides[43-46]. In solvents with a mobile hydrogen atom, an ESR signal was observed in the photolysis of hydroperoxides and their mixtures with peroxides and was attributed to peroxy-radicals from the solvent or the hydroperoxide. In solvents incapable of hydrogenation, a signal due to the peroxy-radicals formed from the hydroperoxide was observed. The absence of signals due to alkoxy-radicals can be explained by their high reactivity which results in their conversion into peroxy-radicals. This is illustrated by the data in Table 5, which lists, for clarity, the rate constants for the interaction of cumenyloxy- and cumenylperoxy-radicals with different substrates.

Table 5. Comparison of the rate constants for the interaction of hydroxy and peroxy-radicals.

Reaction	k, litre mole^{-1} s^{-1}	T°, C	References
RO· + cumene	$2.5 \cdot 10^8$	25	47
RO· + tetralinyl hydroperoxide	$2.0 \cdot 10^6$	25	48
RO· + cumene	0.64	57	49
RO· + tetralinyl hydroperoxide	12.0	67	49

In the photolysis of peroxides in aprotic solvents and sometimes at a low temperature in the absence of oxygen, radicals formed as a result of the decomposition of alkoxy-radicals are observed. For example, the signal due to methyl radicals formed by the reaction

$$(CH_3)_2C_6H_5CO\cdot \rightarrow CH_3\cdot + CH_3COC_6H_5$$

is observed in the photolysis of DCP at 77°K. Thus ESR data agree with the homolytic dissociation of the O—O bond as the primary step in the photolysis of the peroxide, with formation of alkoxy-radicals, which then enter into further reactions.

In certain cases, the ESR method makes possible a more detailed investigation of the step involving the decomposition of the peroxides into radicals[52]. Thus in the photolysis of acyl peroxides from peroxydisuccinic acid, peroxydiglutaric acid, and lauroyl, benzoyl, and acetylbenzoyl peroxides at 77°K (wavelength of irradiating light 300 nm), the ESR spectra consist of broad doublets which are attributed to radical pairs (RP). When a radical pair is exposed to a second light quantum, its constituent radicals emerge from the cage. A six-line spectrum due to the alkyl radicals R· is then observed. The formation of alkyl radicals from acyl peroxides under the influence of light proceeds via the following two-quantum mechanism:

$$R{-}\overset{\overset{O}{\|}}{C}{-}O{-}O{-}\overset{\overset{O}{\|}}{C}{-}R \xrightarrow{h\nu_1} RP \xrightarrow{h\nu_2} R\cdot + CO_2$$

$$[R{-}\overset{\overset{O}{\|}}{C}{-}O\cdot\cdot R]$$

Indeed, it has been established[50-52] that the yield of the radicals R· at 77°K in the photolysis of peroxides of aliphatic acids (butyric, lauric, caproic, and capric) is proportional to the square of the light intensity. Probably these results are related to the low mobility of the radicals in the solid matrix at liquid nitrogen temperature. At higher temperatures, the rate of photochemical decomposition of acyl peroxides is proportional to the light intensity and the fraction of acyl (70%) and alkyl (30%) radicals formed at 20—40°C is independent of temperature[53].

Table 6. Effect of sensitisers on the decomposition of peroxides.

Peroxide	Solvent	Sensitiser	Energy of sensitiser triplet level, kcal mole^{-1}	Effect
Benzoyl peroxide	benzene	acetophenone	73.6	+
ditto	"			
"	cyclohexane	benzophenone	68.5	+
"	benzene	"	68.5	+
"	"	*p*-chlorobenzophenone	68.5	+
"	"	2-acetonaphthone	59.3	+
"	"	penta-2,3-dione	54.7	—
"	"	benzil	53.6	—
"	"	fluorenone	53.3	—
"	"	anthracene	42	+
t-Butyl peracetate	cyclohexane	benzophenone	68.5	+
TBHP	CCl_4	acetophenone	73.6	+
"	CCl_4	benzophenone	68.5	+
"	benzene	"	68.5	+
"	chlorobenzene	"	68.5	+
CHP	cyclohexane	"	68.5	+
Di-t-butyl peroxide	"	"	68.5	—
ditto	benzene		68.5	—

3. Photosensitised Decomposition of Peroxides

Usually the dissociation of the O—O bond in the peroxide requires an energy of less than 40 kcal mole^{-1}. However, the absorption spectra of peroxides suggest that direct decomposition of peroxides requires a considerable amount of energy, of the order of 100—110 kcal mole^{-1} (300—250 nm). Therefore the decomposition of peroxides can occur in sensitised reactions when the sensitiser absorbs light at much longer wavelengths. Photosensitising reactions may be of two types. The absorption of light by the sensitiser can lead to the decomposition of the peroxide into radicals following energy transfer from the sensitiser to the peroxide[54-57] or the sensitiser can propagate the free radical-induced decomposition of the peroxide[58,59]. The sensitisers may be ketones[54,57], aromatic hydrocarbons[55], compounds with condensed nuclei[56], and variable-valence metals[60]. The commonest sensitisers of the

photochemical decomposition of peroxides are various ketones. Table 6 presents data for the effect of ketones on the decomposition of peroxides[56].

Probably sensitisation involves energy transfer from the triplet level of the sensitiser to the peroxide molecule, since the table shows that the sensitisers may be compounds with $n\pi^*$ and $\pi\pi^*$ excited states, where the energy of the triplet level is higher than 55 kcal mole^{-1}. Anthracene, which according to Tsvetkov et al.[68] sensitises the decomposition of peroxides via an excited singlet state with an energy of 76 kcal mole^{-1}, is an exception.

The mechanism of the sensitised decomposition of peroxides can probably be represented as follows[54]:

$$S \xrightarrow[\varphi']{h\nu} S^*$$

$$S^* \xrightarrow{k_d} S$$

$$P + S^* \xrightarrow{k_t} S + P^*$$

$$P^* \xrightarrow{k_d'} P$$

$$P^* \xrightarrow{k_r} \text{products},$$

where S is the sensitiser and P the peroxide. Hence

$$1/\varphi = \left(1 + \frac{k_d'}{k_r}\right)\left(1 + \frac{k_d}{k_t}[P]\right)$$

where φ is the quantum yield of the decomposition of the peroxide.

It has been found for the decomposition of benzoyl peroxide sensitised by benzophenone at room temperature that

$$\frac{k_d}{k_r} = 2.92 \text{ and } \frac{k_d}{k_t} = 0.03 \text{ mole litre}^{-1},$$

i.e. approximately 25% of the peroxide molecules decompose into radicals, while the remaining molecules return to the initial state as a result of the recombination of the radicals in the cage.

4. Photolysis of Polyolefin Hydroperoxides

The study of the photolysis of polymeric hydroperoxides is complicated by the fact that it is virtually impossible to obtain a polymer containing only hydroperoxy-groups[62]. In the low-temperature thermal and photochemical oxidation, hydroperoxy- and carbonyl groups accumulate simultaneously (Fig. 6). Therefore the photolysis of hydroperoxides is always accompanied by the photolysis of ketones.

The ratio of the molar extinction coefficients of hydroperoxides and ketones increases in the long-wavelength part of the spectrum (Fig. 7). Therefore the characteristics of the photolysis of hydroperoxides are clearly shown when they are irradiated with light at a wavelength longer than 365 nm. The decomposition of polypropylene hydroperoxide (PPHP) (at a concentration of 0.1—0.3 M) was observed[28] under these conditions, while the presence of ketones (0.01—0.1 M) in the polymer did not have a significant influence on this process.

As for low-molecular-weight hydroperoxides, the decomposition of polymeric hydroperoxides under the influence of light probably proceeds without an intermediate state. It involves the formation of two radicals, one of which (OH) can readily abstract a hydrogen atom from the polymer with formation of water. Indeed it has been shown[28], that, when PPHP is irradiated with light at a wavelength of 365 nm, each decomposed hydroperoxide molecule results in the formation of one water molecule.



Figure 6. Infrared absorption spectra of oxidised polypropylene films: *a*) oxidation in the melt at 225°C in air, thickness 37 μm: *b*) photochemical oxidation (λ = 370 nm) for 200 h, thickness 40 μm.

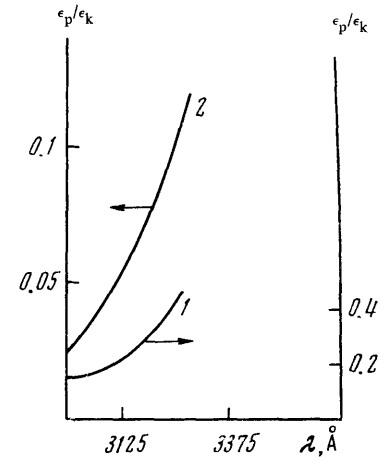
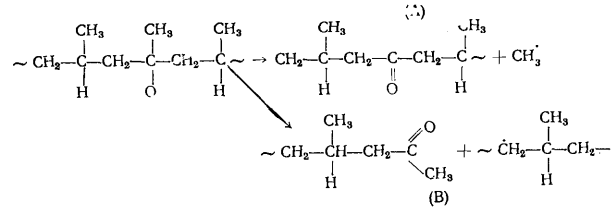


Figure 7. Dependence of the ratio of the molar extinction coefficients of the peroxides and 2,6-dimethylheptan-4-one on the wavelength of the light: 1) di-t-butyl peroxide; 2) t-butyl hydroperoxide.

The radical RO can abstract a hydrogen atom from the polymer with formation of an alcohol and can decompose via the following reactions:



Analysis of the photolysis products of PPHP leads to the conclusion that the ketones (A) and (B) are formed in approximately identical yields. The decomposition of

low-molecular-weight hydroperoxides in solution would result in the preferential formation of the ketone (B).[63,64] This is probably due to the reduced mobility of the high-molecular-weight skeleton of the molecules, which results in a decrease in the quantum yield of the main chain rupture reactions.

The amount of alcohol formed was determined by measuring the absorption in the region of 3400 cm^{-1} (corresponding to the hydrogen-bonded hydroxyls) before and after treating the film with SO_2 in order to remove hydroperoxides[65]. Since the concentration of the hydroperoxide greatly exceeds that of the alcohol, the error in the determination of the latter can be fairly large. However, the data of Carlsson and Wiles[28] indicate its presence in the photolysis products.

Data for the quantitative yield of water in the photolysis of PPHP and the weight loss by the specimen on decomposition of one mole of the peroxide (22 g $mole^{-1}$) show that the photolysis of each hydroperoxy-group gives rise to the formation of one OH· radical and that there is no induced decomposition of the hydroperoxide. This is also indicated by the low yield of the alcohol.

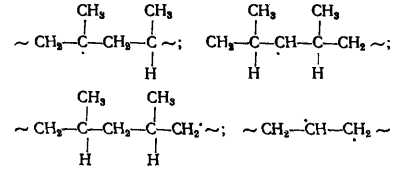
However, at a low temperature, the photolysis of this hydroperoxide is accompanied by the formation of the peroxy-radical $RO_2^{\cdot}$ [66] which can be formed in the absence of oxygen only as a result of the induced decomposition of the peroxide. However, details concerning the removal of oxygen dissolved in the polymer film are not given in Ershov's paper[66]. Possibly the $RO_2^{\cdot}$ radical is formed from the RO· or R· radical by reaction with oxygen. Thus the question of the induced decomposition of PPHP remains open. In the study of Carlsson and Wiles[28], the quantum yield of the decomposition of PPHP was found to be 4.0 ± 0.5, which the authors attribute to the difference between the molar extinction coefficients of PPHP and t-butyl hydroperoxide, the spectrum of which was used to determine the amount of absorbed light.

Sensitised decomposition by the ketones present in the polymer is not observed in the decomposition of PPHP under the influence of light at a wavelength of 365 nm. The quantum yield of the decomposition of the peroxide does not change when the concentration of ketones is altered almost by a power of ten. Thus the photolysis of PPHP occurs with a decomposition quantum yield close to unity with formation of alkyl radicals (polymeric or $CH_3^{\cdot}$), a ketone, and hydroxyl-radicals. The latter give a quantitative yield of water and alkyl radicals. The alkyl radicals probably do not recombine with one another, as shown by the small change in the molecular weight of the polymer during irradiation.

Very small amounts of methane and ethane, formed in different reactions of methyl radicals, were detected in the volatile photolysis products.

5. Radical Formation in Polyolefins

Degenerate branching of the photochemical oxidation chains occurs in those reactions of hydroperoxides and ketones where they give rise to free radicals. The formation of free radicals in the photolysis of polyolefins at low temperatures can be detected by the ESR method. However, sufficient data are not yet available for a quantitative comparison of the compositions of the photolysis products of oxidised polyolefins with the quantum yields for radical formation in these processes. The majority of studies on the amounts and structures of the radicals formed have been made with γ-irradiated specimens[68-70] and the effect of ultraviolet irradiation on polyolefins has been investigated very much less thoroughly[71-73]. When polyethylene is irradiated with ultraviolet light (77°K, total light of a mercury lamp) *in vacuo*, a signal, consisting of a mixture of a sextet (with a splitting of 21 G) and a quintet (with a splitting of 120 G) is observed. By analogy with data obtained for γ-irradiated specimens, the sextet is attributed to the radical $CH_2-\dot{C}H-CH_2$ and the quintet to the terminal radical $-CH_2-\dot{C}H_2$. The latter is detected only when polyethylene is irradiated by ultraviolet light; in particular it can be the radical formed by the photolysis of carbonyl compounds. When polypropylene is irradiated with ultraviolet light, a signal, consisting of two superimposed quartets with a splitting of 23 G is observed[24,67,71,73,74]. The narrower of the quartets refers to the methyl radical CH_3 and the second, broader, and more diffuse quartet refers to a mixture of radicals:



As with the γ-irradiated polymers, the fraction of each radical was not determined. When the irradiated polymer is heated to 178°K for 10 min, approximately 40% of the initial concentration of radicals remain, while on heating to room temperature all the radicals vanish[71]. On repeated irradiation of the specimen by light at wavelengths less than 270 nm, the broad signal of the polymeric radicals is partly converted into the narrower signal of methyl radicals[24].

When partly oxidised polypropylene is irradiated *in vacuo*[24,67,75], a complex asymmetric signal is observed, in which the singlet line of an oxygen-containing radical (RO· according to the authors) predominates. At the same time alkyl radicals are formed in the system. The fraction of each of these radicals and the quantum yields for their formation were not determined.

Unfortunately in all the studies quoted above the nature of the absorbing centres in the polyolefins and their role in the accumulation of radicals in the polymer were not investigated. Admittedly, the accumulation of radicals in oxidised polypropylene has been attributed[75] to the photolysis of hydroperoxides but the role of the keto-groups inevitably present in the polymer was not taken into account quantitatively.

Some investigators[3,24] believe that the absorbing centres in polyolefins responsible for radical formation are admixtures of aromatic hydrocarbons—naphthalene, anthracene, phenanthrene, etc., known to be photosensitisers of the ageing of polymers[4]. According to their data, the ESR spectrum obtained on irradiation of polypropylene with ultraviolet light in the presence of added phenanthrene agreed fully with the ESR spectrum of irradiated commercial polypropylene[24].

The differences between the ESR spectra of oxidised polypropylene and polypropylene containing photosensitising impurities are probably associated with the difference between the reactivities of the primary excited molecules or radicals obtained on low-temperature irradiation (77°K). The composition of the photolysis products of oxidised polypropylene shows that at higher temperatures methyl and alkyl radicals are also formed in the polymer[28].

In the photosensitised degradation of polypropylene, the initial rate of radical formation is proportional to the square of the light intensity[3,24]; this can be accounted for

by the transition of the impurity to a photochemically active state in a two-quantum process proceeding via a triplet state. The formation of radicals in polyolefins sensitised by aromatic compounds can probably be regarded as a result of transfer of excitation energy from the highest triplet levels of the sensitiser to the matrix or as a result of a two-quantum degradation of the sensitiser with subsequent reaction between the products and the polymer[76,77].

Naturally, similar two-quantum processes play a significant role at a low temperature and a high light intensity. The extrapolation of these data to natural conditions must be performed with much caution.

The free radicals formed in polyolefins under the influence of light can undergo various interconversions. Thus polymeric alkyl radicals can be converted into allyl radicals under the influence of the light of a xenonormercury lamp. The mechanism of this process has not so far been established. It is only known that the reaction is reversible and the reverse process was investigated in fair detail[78,79].

Photolysis of polymeric alkyl radicals by light at wavelengths less than 270 nm and low temperature leads to the formation of methyl radicals[24,89]. Photolysis of polymeric peroxy-radicals by light at wavelengths greater than 280 nm and also at low temperature yields an excited peroxy-radical which abstracts a hydrogen atom from the polymer and gives rise to a hydroperoxide and an alkyl radical via the reactions[89]

$$RO_2^{\cdot} + h\nu_{<280} \rightarrow RO_2^{*},$$
$$RO_2^{*} + RH \rightarrow [RO_2H + R^{\cdot}],$$

Under the influence of short-wavelength light (<280 nm), a peroxy-radical is probably formed in another excited state $RO_2^{*'}$ or the product is an exciplex decomposing into radicals:

$$RO_2^{\cdot} + h\nu_{<280} \xrightarrow{RH} [RO_2^{*'} + RH] \rightarrow \dot{R} + \dot{R}O + \dot{O}H \xrightarrow{+RH} 2\dot{R} + \dot{R}O + H_2O$$

i.e. in this case the photolysis of the peroxy-radical leads to branching of the oxidation chain.

Close to room temperature, appreciable concentrations of free radicals are not detected when polyolefins are irradiated by light under any conditions, i.e. the lifetimes of the radicals are then short. All the photochemical reactions of radicals are secondary photochemical processes and therefore their role can be appreciable only when the lifetime of the radical is long. Consequently the role of these processes in the photochemical oxidation of polyolefins is insignificant.

Thus one can regard it as established that free radicals are formed in the initiation steps and in the degenerate branching of the photochemical chain oxidation of polyolefins. There have not yet been any rigorous quantitative studies permitting the determination of the nature of the radicals and the quantum yields of the radical formation processes and enabling the role of the two-quantum processes and the photolysis of the polymeric radicals formed to be taken into account. However, the principal features of the reactions occurring in the degenerate branching step of the polyolefin photochemical oxidation chain are clear.

Hydroperoxides with an absorption spectrum of the type shown in Fig. 5 are decomposed with a quantum yield close to unity. The occurrence of sensitised decomposition of hydroperoxides has not been established exactly. The terminal and central aliphatic ketones have approximately identical absorption spectra (Fig. 3) and accumulate during the oxidation process in approximately equal concentrations. The average quantum yield of their photochemical decomposition is close to 0.1. Each ketone molecule decomposed yields on average of one alkyl radical and one molecule of another ketone with a single break in the chain of the polymer molecule.

In the presence of an excess of oxygen, all the alkyl radicals are converted into peroxy-radicals and, apart from the peroxy-radical, each alkoxy-radical gives rise to one ketone molecule and each hydroxy-radical yields a water molecule.

As a result, the degenerate chain branching stage in the photochemical oxidation can probably be represented as follows:

$$POOH + h\nu - PO + OH \xrightarrow{2O_2+2PH} H_2O + K + 2PO_2,$$
$$K + h\nu \xrightarrow{+O_2} PO_2 + K + S(=),$$

where POOH is the polymer hydroperoxide, PO and PO_2 are the alkoxy- and peroxy-radicals of the polymer, K is the ketone, and S(=) represents compounds with a double bond.

IV. PROPAGATION AND TERMINATION OF OXIDATION CHAINS

The chain propagation and termination stages in the photochemical oxidation of polyolefins probably do not differ from the analogous reactions in thermal oxidation and proceed without the involvement of light. Both these stages in the thermal oxidation of polyolefins have now been discussed in the literature[90-92], but we are not aware of analogous studies on photochemical oxidation. The oxidation chain propagation and termination stages can be best investigated separately in the course of sensitised oxidation. The kinetic mechanism of this process in the presence of an excess of oxygen can be represented by the following set of reactions:

$$\begin{aligned} &Y \xrightarrow{w_i} \dot{r} \xrightarrow{(O_2)} R \ (1) \text{ chain initiation},\\ &RO_2 + RH \xrightarrow{k_p} RO_2H + \dot{R} \ (2),\\ &R + O_2 \xrightarrow{k_p'} RO_2 \ (3) \text{ chain propagation},\\ &RO_2^{\cdot} + RO_2^{\cdot} \xrightarrow{k_t} (4) \text{ quadratic chain termination}, \end{aligned} \qquad (I)$$

where Y is a sensitiser decomposing into radicals at a rate w_i and k_p and k_t are the rate constants for chain propagation and termination.

The rate of oxidation w is determined by the rate of chain propagation. Therefore the rates of accumulation of hydroperoxides in reaction (2) and of absorption of oxygen in reaction (3) determine the value of w:

$$w = \frac{d(\text{ROOH})}{dt} = \frac{d(O_2)}{dt} - nw_i = \frac{k_p}{\sqrt{k_t}}\sqrt{w_i}(\text{RH})$$

where nw_i is a term taking into account the absorption of oxygen in the chain initiation step and its evolution in the chain termination.

However, it is hard to study the pure sensitised oxidation of polyolefins because it is difficult to introduce sensitisers capable of decomposing into free radicals at a sufficiently low temperature where the principal branching agents (hydroperoxides) do not decompose. There have been only two investigations where studies of this kind were made, namely the oxidation of atactic polypropylene and an ethylene—propene copolymer (with benzoyl peroxide as a sensitiser) in the temperature range 85—110°C [93] and the oxidation of low-pressure polyethylene (with DCP as an initiator) at 110—130°C.[94] The parameters $k_p/\sqrt{k_t}$ found are listed in Table 7.

Table 7. Rate constants for chain propagation and termination in the oxidation of polypropylene.

T, °C	k_p, litre mole^{-1} s^{-1} from Ref.95	k_t, 10^6 litre mole^{-1} s^{-1} from Ref.92	$k_p/\sqrt{k_t}$, 10^{-3} litre mole^{-1} s$^{-1/2}$ from Ref.92	from Ref.90	from Ref.93*	from Ref.94*
110	1.9	6.2	0.76	—	—	—
120	3.3	9.0	1.1	0.56	5.6	0.22**
130	4.2	9.0	1.4	0.86	—	—
140	4.6	6.6	1.8	1.4	—	—
E_a, kcal mole^{-1}	0	0	9	12.8	17	21.3

*These values of $k_p/\sqrt{k_t}$ were obtained in the sensitised oxidation of polymers.
**Low-pressure polyethylene.

The chain propagation and termination rate constants for polyolefins were obtained mainly in studies on degenerate branched-chain thermal oxidation. Degenerate branched-chain oxidation and unimolecular chain branching and quadratic termination reactions have been discussed[95]. The accumulation of the peroxide and the absorption of oxygen in such a system in the initial stages is described by a parabola in accordance with equations (5) and (6):

$$ROOH = ROOH_\infty (1 - e^{-\frac{k_0}{2}t})^2 \simeq ROOH_\infty \left(\frac{k_0}{2}t\right)^2, \quad (5)‡$$

$$\Delta O_2 = ROOH_\infty (2k_0 t - (5 - e^{-\frac{k_0}{2}t})(1 - e^{-\frac{k_0}{2}t}) \simeq ROOH_\infty \left(\frac{k_0}{2}t\right)^2, \quad (6)$$

where $ROOH_\infty$ is the limiting concentration of the peroxide and k_0 is the hydroperoxide decomposition rate constant.

It has been shown[90,91] that the thermal oxidation of polypropylene in the initial stage does indeed obey Eqns.(5) and (6) and at more advanced stages of the reaction, where the consumption of the polymer oxidised cannot be taken into account, the rate of oxidation decreases according to the law

$$\frac{1}{RH_0 - \Delta O_2} = 2\frac{k_p^2}{k_t}t + \text{const.} \quad (7)$$

Eqns. (5)—(7) make it possible to determine the same parameter $k_p/\sqrt{k_t}$ from the initial section of the kinetic curve and from the section where the concentration of the peroxide reaches a limiting level. The values of the parameter $k_p/\sqrt{k_t}$ found by these two procedures agree, which demonstrates the validity of the mechanism employed.

The absolute values of the constants k_p and k_t have been determined[84]. In the same study, the rate of steady-state autoxidation of polypropylene after the induction period was investigated. Under these steady-state conditions, measurements were made of the rate of absorption of oxygen $(dO_2/dt)_s$ and of the concentration of the hydroperoxide $(ROOH)_s$ and it was found that the decomposition of the peroxide in the formation of two radicals:

$$k_p = (-dO_2/dt)_s/(RO_2)(RH),$$
$$k_t = (-dO_2/dt)_s/2(RO_2)^2,$$

Table 7 list the values of k_p, k_t, and of the parameter $k_p/\sqrt{k_t}$ obtained. For comparison, the parameter $k_p/\sqrt{k_t}$ for polyethylene is also included. This value agrees well with the corresponding parameter for 1,3,5-trimethylpentane[96]:

$$\frac{k_p}{\sqrt{k_t}} = 8 \cdot 10^{-4} \text{ litre mole}^{-1}\text{ s}^{-1/2} (130°).$$

‡ Eqns. (1)—(4) are missing in the Russian original (Ed. of Translation).

The activation energy for the parameter $k_p/\sqrt{k_t}$, determined in the temperature range 110—140°C, is approximately 10 kcal mole^{-1}, which is also close to the corresponding value for low-molecular-weight compounds. Thus the chain propagation and termination stages in the oxidation of polyolefins above 100°C proceed in the same way as for low-molecular-weight compounds in the liquid phase.

At 200—250°K the kinetics of the destruction of radicals should not be determined by their chemical reactivity but by their mobility in the polymer matrix[88,89]. Therefore at a somewhat higher temperature, close to room temperature, the specific features of the solid phase can presumably also influence significantly the mechanisms of the chain propagation and termination reactions. However, we are unaware of any studies in which a detailed investigation was made of the influence of the specific features of the solid phase on the mechanism of the oxidation of polyolefins. One can only point to a study where a relation between the kinetics of the thermal oxidation of polypropylene and the supermolecular structure of the specimen was observed[97].

V. CHARACTERISTICS OF THE OXIDATION OF POLYMERS

The above discussion of the principal stages in the oxidation of polymers showed that, as in the oxidation of low-molecular-weight compounds, the principal products of the oxidation of polyolefins are peroxides, ketones, alcohols, and ethers. However, the great length of the polymer chain is responsible for certain specific features of the structure of these compounds. For example, polypropylene oxidised in a solution containing a sensitiser consists of "blocks" which incorporate between two and eight hydroperoxy-groups[98]. Data for the distribution of the hydroperoxy-groups in the blocks have been obtained by analysing the ultraviolet spectra of polyenes obtained from the hydroperoxide via the mechanism

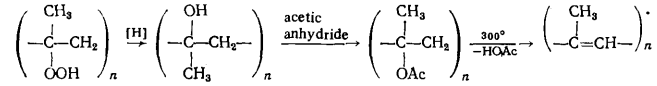
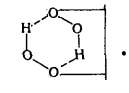


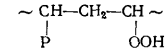
Fig. 8 presents data on the distribution of "adjacent" (located at neighbouring carbon atoms) hydroperoxy-groups in polypropylene hydroperoxide. The figure shows that the majority of the blocks contain two hydroperoxide groups. PPHP does not contain any isolated hydroperoxy-groups[98].

Analysis of the infrared absorption spectra of PPHP showed in addition that more than 90% of the hydroperoxy-groups are linked by hydrogen bonds. The PPHP structure can be represented as follows:



This structure shows that in each block with an odd number of groups one hydroperoxy-group is involved in hydrogen bonding.

By analogy with these data, it is believed[99] that isolated hydroperoxy-groups are also not encountered in polyethylene hydroperoxide (PEHP). The structure of PEHP can be represented by the formula



where P is a hydroxy- or carbonyl group. This structure of polyolefin hydroperoxides is consistent with ESR data. It has been noted[100] that the form of the ESR line associated with peroxy-radicals in polypropylene and polyethylene hardly changes with temperature in the range between −200° and 100°C. On the other hand, in Teflon, for example, the line form does depend significantly on temperature[101]. This result implies that the O—O group in polyolefins remains immobile in the temperature range investigated. The authors attribute this to the fact that fairly strong hydrogen bonds, capable of fixing the O—O group in a specified position, are formed in polypropylene and polyethylene.

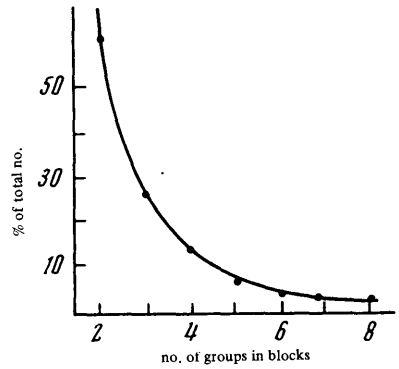


Figure 8. Distribution of hydroperoxy-groups in the blocks of oxidised polypropylene.

Table 8. Rate constants for reactions determining the kinetics of the decomposition of polyolefin hydroperoxides.

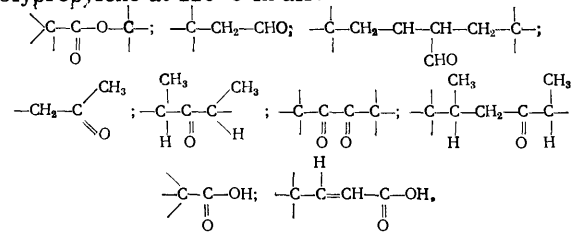
T, °C	k_{fast}, s^{-1}		k_{slow}, s^{-1}	E_{act}, for fast reactions, kcal $mole^{-1}$	
	from Ref.99	from Ref.103	from Ref.99	from Ref.99	from Ref.103
Polyethylene hydroperoxide					
110	$3.2\cdot10^{-5}$	$4.4\cdot10^{-4}$	—	—	—
110	—	$6.6\cdot10^{-4}$	—	20	25
120	$1.7\cdot10^{-4}$	$9.1\cdot10^{-4}$	$1.4\cdot10^{-5}$	—	—
	from Ref.102		from Ref.102	from Ref.102	
Polypropylene hydroperoxide					
85	0.33		—	—	
100	0.87		—	—	
120	5.01		4.32	25	
135	19.8		—	—	

This structure of the polymer oxidation products is associated with the fact that the oxidation proceeds to a considerable degree via an intramolecular mechanism in the presence of a high local concentration of oxidation products. The presence of several functional groups in the immediate vicinity of one another within a single macromolecule alters their properties and reactivities. For example, thermal decomposition of PPHP and PEHP *in vacuo* proceeds according to a complex law and can be represented by two consecutive unimolecular reactions with rate constants differing by more than a power of ten[90,99,102,103]. Table 8 presents the rate constants for the slow and rapid stages of the decomposition of PPHP and PEHP.

The faster stage of the decomposition of the hydroperoxide is attributed to the decomposition of the hydroperoxy-groups linked by hydrogen bonds to similar OOH groups[99,102]. The slow stage is attributed to the decomposition of a β-hydroxyhydroperoxide. This interpretation is supported by the increase in the fraction of hydroperoxy-groups, undergoing a slower decomposition at more advanced stages of the hydroperoxide decomposition process and also in the presence of oxidation inhibitors, for example 2,6-di-t-butyl-*p*-cresol[102]§.

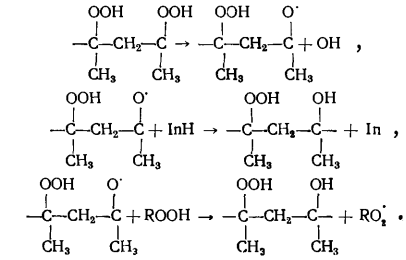
The rate constants for both stages of the decomposition of polyolefin hydroperoxides in solution and in crystalline and amorphous polymers are similar. This confirms that the decomposition of the hydroperoxide proceeds intramolecularly. The bulk of the polymer oxidation products are obtained as a result of further reactions of the hydroperoxides, the structures of the products being determined by the characteristics of the hydroperoxide structures. For example, the infrared spectra of oxidised polypropylene have a broad band in the region of absorption by the carbonyl group (1720 cm^{-1}), which, as already stated, is a result of a superposition of the absorption bands due to several ketones (Fig. 6).

By interpreting their spectra on a computer, Carlsson and Wiles[28] established that at least 9 ketones are formed in polypropylene at 220°C in air:



This result is probably not entirely unambiguous, since Adams[104] obtained a similar spectrum, which he interpreted as a result of the superposition of the absorption bands of ketones, aldehydes, acids, esters, and γ-lactones. At present it is apparently difficult to specify exactly the composition of the polyolefin oxidation products. Presumably they include two ketones corresponding to the location of the C=O groups at the end and in the middle of the chain and having absorption maxima at 1718 and 1726 cm^{-1} respectively.

§ In both these cases, the β-hydroxyhydroperoxide accumulates at a comparatively high concentration as a result of the reaction



Even the qualitative composition of the products accumulated in the polymer depends on its oxidation conditions. For example, under the conditions of the industrial processing of olefins (at about 200°C), polyolefin hydroperoxides decompose almost completely and from the entire range of oxidation products polymeric ketones are mainly obtained. At a lower temperature, considerable amounts of peroxides accumulate in the polymers[62,90,92]. However, it is almost impossible, as already stated, to obtain the pure polymeric peroxide by the oxidation reaction. It is always accompanied by decomposition products (ketones)[62].

VI. KINETICS OF THE PHOTOCHEMICAL OXIDATION OF POLYOLEFINS

The above discussion of the individual stages of the photochemical oxidation of polyolefins showed that the kinetic mechanism II of this process can be formulated as follows:

$$S_1 + h\nu \rightarrow PO_2 \quad (8)$$

$$POOH + h\nu \rightarrow PO^{\cdot} + OH^{\cdot} \xrightarrow{2O_2+2PH} 2PO_2 + H_2O + K \quad (9)$$

$$K + h\nu \xrightarrow{2O_2} (PO_2) \text{ for } (K + S(=)) \quad (10)$$

(II)

$$PO_2 + PH \xrightarrow[k_p]{O_2} POOH + PO_2 \quad (11)$$

$$PO_2 + PO_2 \xrightarrow{k_t} K + POH + O_2 \quad (12)$$

where S_1 is the sensitising impurity in the polymer PH.

The photochemical oxidation of polymers which hardly absorb light thus differs from the thermal oxidation only by a greater complexity of the degenerate chain branching and chain termination steps. The kinetics of this process can be described by the following set of differential equations:

$$\frac{d(POOH)}{dt} = -\frac{\alpha I_0 (POOH)}{2} + \frac{k_p}{\sqrt{k_t}} \Pi H \sqrt{(\alpha POOH + \alpha_1 K + \alpha_0 S) I_0}, \quad (13)$$

$$\frac{d(O_2)}{dt} = (\alpha POOH + \alpha_0 S + \alpha_1 K)\frac{I_0}{2} + \frac{k_p}{\sqrt{k_t}} pH \sqrt{(\alpha POOH + \alpha_1 K + \alpha_0 S) I_0}, \quad (14)$$

$$\frac{dK}{dt} = \alpha I_0 POOH \quad (15)$$

where the coefficients α_0, α, and α_1 are products of the molar extinction coefficient and the quantum yield for the formation of free radicals in the photolysis of the impurity, the peroxide, and the ketone respectively.

Eqns. (13)—(15) become identical with Eqns. (5) and (6) describing the thermal oxidation of polyolefins when $\alpha_1 = 0$. The solution becomes particularly simple when $\alpha_0 = 0$; then, in the absence of photolysis of impurities, the mathematical description of the process becomes analogous to the description of the thermo-oxidative degradation given by Pudov[90]:

$$\frac{POOH}{POOH_\infty} = (1 - e^{-\frac{\alpha I_0}{4} t})^2,$$

$$\frac{K}{POOH_\infty} = \alpha I_0 t - 2(3 - e^{-\frac{\alpha I_0}{4} t})(1 - e^{-\frac{\alpha I_0}{4} t}), \quad (16)$$

$$\frac{\Delta O_2}{POOH_\infty} = \alpha I_0 t - (5 - e^{-\frac{\alpha I_0}{4} t})(1 - e^{-\frac{\alpha I_0}{4} t}),$$

where

$$POOH_\infty = \frac{4k_p^2 PH^2}{\alpha k_t I_0}$$

is the limiting concentration of the peroxide which can accumulate in the system. The equations show that the concentration of the reactants initially increases autocatalytically according to a parabolic law:

$$\frac{\Delta O_2}{POOH_\infty} \simeq \frac{POOH}{POOH_\infty} \simeq \left(\frac{\alpha I_0}{4} t\right)^2, \quad \frac{K}{POOH_\infty} \simeq \frac{2}{3}\left(\frac{\alpha I_0}{4} t\right)^3; \quad (16')$$

After a time of the order of $0.2/\alpha I_0$, a significant concentration of the peroxide accumulates, whereupon after a time $t = 4 \ln 2/\alpha I_0$ the rate of accumulation of the hydroperoxide reaches its maximum value $\alpha I_0 (POOH)_\infty/8$ and after a time of the order of $10/\alpha I_0$ its concentration reaches a steady-state value.

The steady-state concentration of the peroxide is inversely proportional to the light intensity, but it is attained faster at higher light intensities. This is illustrated by the data in Fig. 9, which presents kinetic curves for the accumulation of the peroxide calculated from Eqn. (16) for light intensities differing by a factor of 100.

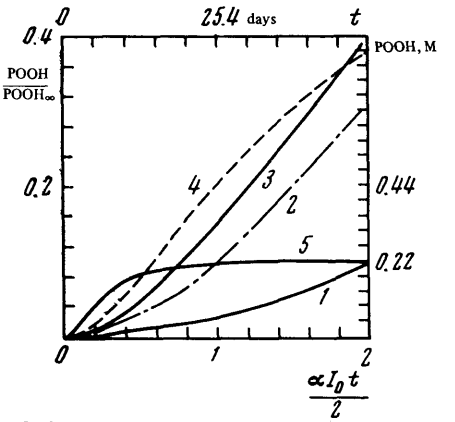


Figure 9. Calculated kinetic curves for the accumulation of peroxides at different incident light intensities: 1) $0.1\,I_0$; 2) $0.5\,I_0$; 3) I_0; 4) $2\,I_0$; 5) $10\,I_0$; $POOH_\infty$ corresponds to curve *3*. The right-hand and upper scales correspond to $I_0 = 10^{16}$ quanta s^{-1} cm^{-2} (365 nm monochromatic light of PRK-7 lamp 6 cm from the centre). The extinction coefficient of the peroxide at 365 nm is 0.012 litre $mole^{-1}$ cm^{-1}.

The kinetic curves for the accumulation of peroxides and carbonyl groups and for the absorption of oxygen in the course of the photochemical oxidation are presented in Fig. 10. At the beginning of the process, the entire absorbed oxygen is used to form the peroxide; along this section, the kinetic curves *1* and *2* coincide. At more advanced stages of the oxidation process, the kinetic curves for the absorption of oxygen remain parabolic, while the accumulation of peroxides slows down, since their decomposition becomes significant. At roughly this time, relatively high concentrations of ketones accumulate.

The kinetic curve for the accumulation of ketones in the initial stages is close to a cubic parabola. After this,

as the concentration of the peroxide reaches its steady-state value, the rates of absorption of oxygen and of accumulation of carbonyl compounds also reach their steady-state values, which are equal. The kinetic curves in Figs. 9 and 10 were calculated for the condition where the polymer is free from impurities and does not absorb light in the first instants. Thus one can calculate the kinetic curves for the photochemical oxidation of "ideally" purified polyolefins, which is, so to speak, the curve for the slowest photochemical oxidation of polyolefins.

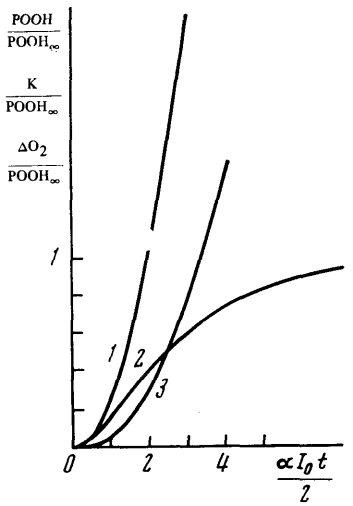


Figure 10. Calculated kinetic curves for the absorption of oxygen (curve *1*) and the accumulation of peroxides (curve *2*) and carbonyl groups (curve *3*) in photochemical oxidation.

We attempted to perform such a calculation for a real system. Fig. 9 presents the kinetic curve for the accumulation of peroxides in thoroughly purified isotactic polypropylene (curve *3*, the upper and right-hand side scales) on irradiation with light corresponding to the 365 nm line of the PRK-7 lamp at a distance of 7 cm from the source. The parameter $k_p/\sqrt{k_t}$ was calculated by extrapolating Chien and Ross's data[92] to a low temperature. Fig. 9 shows that under such conditions significant concentrations of the peroxide can accumulate in the purified polypropylene over a period of the order of one month.

The conditions $\alpha_1 = 0$ and $\alpha_0 = 0$ are fulfilled when polyolefins are irradiated with long-wavelength light whose spectral composition is close to that of sunlight [ketones do not absorb sunlight (Fig. 3) and, as shown above, impurities can have a significant influence only on the initial sensitisation].

If the sensitising impurity is not consumed in the course of the process, then its effect in the initial stage is characterised by the parameter

$$\varphi = \frac{\sqrt{\alpha_0 s I_0 k_t}}{k_p \mathrm{PH}} .$$

The initial stage of the accumulation of the peroxide is described in this case by the equation

$$\frac{\mathrm{POOH}}{\mathrm{POOH}_\infty} = \varphi \alpha I_0 t + \frac{1}{4}\left(\frac{1}{4} + \varphi\right)(\alpha I_0 t)^2 .$$

Fig. 11 presents rigorous solutions of Eqns. (13)–(15) for different values of the parameter $\varphi = \sqrt{\alpha_0 I_0 k_t s}/k_p \mathrm{PH}$. Evidently the quantity φ, characterising the role of extraneous impurities, has the greatest influence in the initial stages of the process and, when $\varphi \ll \alpha I_0 t/16$, it can be neglected. It is difficult to say anything about the value of φ owing to the wide variety of impurities in polyolefins, but, as stated above, the appreciable self-acceleration of the photochemical oxidation process suggests that it is small and decreases with time owing to the consumption of the impurity.

The absorption of light by ketones begins to be appreciable at advanced stages of the photochemical oxidation process and can be neglected when

$$I_0 \alpha t \ll \frac{(3 \div 4)\,\alpha}{\alpha_1} .$$

The ratio α_1/α is probably close to unity, since the extinction coefficient of ketones in the long-wavelength part of the spectrum is higher approximately by a power of ten than that of peroxides and the quantum yield of their decomposition into radicals is lower by a factor of 10–20 (data of Carlsson and Wiles[28,62] and Figs. 3 and 5). Thus the sections of the curves for the accumulation of peroxides up to the point of inflection should be described by Eqn. (7) for highly purified polymers.

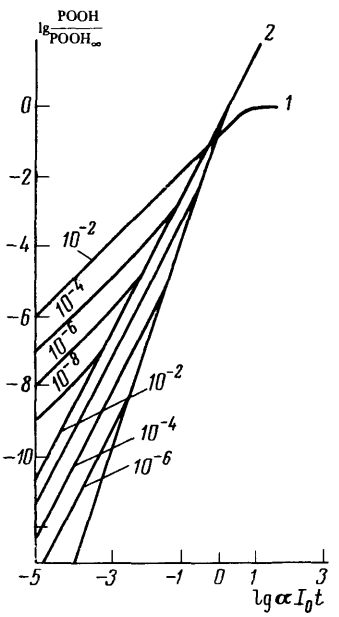


Figure 11. Logarithmic kinetic curves for the accumulation of peroxides (curve *1*) and ketones (curve *2*) in photochemical oxidation for different values of φ.

Unfortunately we were unable to find any studies in which a kinetic analysis of the photochemical oxidation of polyolefins has been carried out. Some investigators observed the accumulation of carbonyl groups in the course of photochemical oxidation and described it by an exponential relation[12] or by a curve with an induction period[13,14]. In all cases interpretation of the data quoted

permits their satisfactory description by a quadratic and cubic parabola within the framework of mechanism (II) quoted above, which corresponds to Eqns. (8)—(12). Fig. 12 presents experimental kinetic curves for the accumulation of carbonyl compounds in the photochemical oxidation of atactic polypropylene[13]. It also includes curves calculated from Eqns. (13)—(15).

For a quantitative description of the kinetics of the photochemical oxidation of polyolefins with the aid of Eqns. (13)—(15), it is necessary to know the spectral composition and absolute intensity of the light sources employed as well as the value of the parameter $k_p/\sqrt{k_t}$. It is then possible to make a quantitative calculation of the kinetic curves for the accumulation of peroxides and carbonyl compounds and for the absorption of oxygen. However, comparison of such calculation with experimental data involves certain difficulties. This is because the parameter $k_p/\sqrt{k_t}$ has not been measured at room temperature and its calculation by extrapolation of the data obtained at higher temperatures can lead to considerable errors. On the other hand, in many reports the necessary data concerning experimental conditions are lacking. Nevertheless we attempted to compare the kinetic curves for the accumulation of carbonyl compounds in the oxidation of polypropylene taken from Balaban et al.[12] with the calculated results; the parameter $k_p/\sqrt{k_t}$ was obtained by extrapolating Chien and Ross's data[92] to 30°C ($k_p/\sqrt{k_t} = 3.6 \times 10^{-5}$ litre mole^{-1} s^{-1}); the probability of the absorption of light quanta by a peroxide molecule ($\int \epsilon I d\lambda$) ^{105} was calculated from the absorption spectra of the light filters employed, the emission spectrum of the light source, and the absorption spectrum of the peroxide (Fig. 5), which are quoted by Melchore[13].

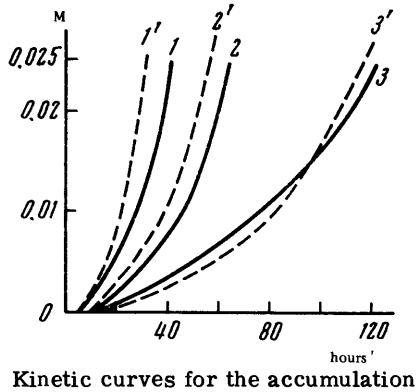


Figure 12. Kinetic curves for the accumulation of carbonyl compounds in the photochemical oxidation of atactic polypropylene[13]: 1)—3) from Melchore's data[13]; 1')—3') calculated data [1) without a filter; 2) and 3) with different light filters].

If the parameter $k_p/\sqrt{k_t}$ is calculated from the results of Pudov and coworkers[90,91], the accumulation of carbonyl compounds is found to be slower than in the experiments.

Thus Eqns. (13)—(15) apparently give a correct prediction of the scale of the phenomenon. However, in order to test rigorously the validity of mechanism (II), it is necessary to carry out special investigations.

It follows from Eqns. (13)—(15) that the dependence of the induction period, determined from the absorption of oxygen τ_{O_2}, the accumulation of the peroxides τ_{ROOH}, or the accumulation of ketones τ_K on light intensity and temperature is qualitatively different in each case. At the beginning of the process the induction period based on the accumulation of peroxides τ_{ROOH} is inversely proportional to the square root of the light intensity and corresponds to the same activation energy E_{ROOH} as the parameter $k_p/\sqrt{k_t}$. The induction period based on the accumulation of ketones is inversely proportional to $I^{2/3}$ and corresponds to the activation energy $(2/3)E_{ROOH}$. Indeed it has been shown[14] that the activation energy associated with τ_{ROOH} is 7 kcal mole^{-1}, which is close to the activation energy associated with the parameter $k_p/\sqrt{k_t}$, measured by Chien and Ross[92] (9 kcal mole^{-1}).

On the other hand, if the sensitivity of the method used to determine peroxides or ketones is relatively low, deviations from the above relations may be observed. It has been shown[12] that the induction period for the accumulation of ketones (τ_K) is inversely proportional to the square root of the light intensity. A small discrepancy may be due to the fact that degenerate chain branching owing to the photochemical decomposition of ketones, occurring because the irradiation was carried out with the unfiltered light of the mercury lamp, had an appreciable influence on this process.

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Institute of Chemical
Physics, USSR
Academy of Sciences,
Moscow

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Advances in the Synthesis of 3,7,9-Heteroanalogues of Bicyclo[3,3,1]nonane

N.S.Zefirov and S.V.Rogozina

The heteroanalogues of bicyclo[3,3,1]nonane are of great theoretical and practical interest, which has stimulated synthetic studies in this field. These compounds are used as physiologically active substances and as intermediate in organic synthesis (for example in the synthesis of heteroadamantanes); a heterobicyclononane fragment occurs in the structures of certain alkaloids. The compounds are convenient models for stereochemical and conformational studies.
Despite the very large number of novel studies on the synthesis of compounds of this type, relevant reviews are not available. The present review gives a systematic analysis of typical mechanisms of the synthesis and the synthetic scope of each method and the limits of its applicability are discussed.
The bibliography includes 140 references.

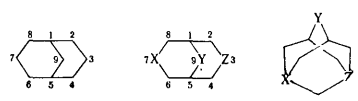
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1. INTRODUCTION

Bicyclic and skeletal compounds are now attracting increased attention owing to their unique physical or chemical properties, which makes them interesting models for the study of theoretical problems in conformational analysis, the mechanisms and the stereochemistry or reactions, the transmission of electronic effects, etc. Heteroanalogues of bicyclic systems are of special interest. The introduction of heteroatoms usually involves the retention of the general geometry characteristic of the parent hydrocarbon but can greatly modify the physical properties or the chemical behaviour of the functional groups. In many cases this leads to an extension of the range of unusual properties, which increases the scope of the application of these compounds both in theoretical studies and for important practical purposes, for example as physiologically active substances. As an example, one can point to studies using heteroanalogues of norbornane [1-4] which is one of the most widely used model compounds in theoretical studies.

This review deals with methods of synthesis of heteroanalogues of one of the bicyclic systems—bicyclo[3,3,1]-nonane (I). Derivatives of this compound are finding many applications both in conformational studies [5-10] and for synthetic purposes [11-14].



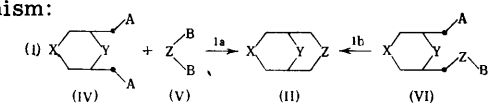
(I) (II) (III)

The methods of synthesis of bicyclo[3,3,1]nonanes are discussed exhaustively in a new review [15] and there is an extremely large literature on the synthesis of heteroanalogues of this series. Here we shall confine ourselves to a discussion of compounds with heteroatoms in the 3-, 7-, and 9-positions [compounds(II)]. Apart from the limited amount of space available, this restriction is based both on the great theoretical importance of heteroanalogues of this type and on their extensive synthetic applications, in particular in the synthesis of adamantane structures of type (III). [11-14,16-18] We may also emphasise that the 3(7)- or 9-azabicyclo[3,3,1]nonane fragment occurs in the structures of many natural alkaloids. For example, 3,7-diazabicyclononane occurs in the skeleton of alkaloids in the plant family *Papilionaceae*: lupanine, sparteine, and anagyrine; the 3-azabicyclononane fragment also occurs in the structure of certain diterpene alkaloids [20]; a series of alkaloids are also based on the 9-azabicyclononane fragment [19,21]. Special mention should also be made of the use of these compounds as physiologically active agents. Thus 3-oxa-9-azabicyclo[3,3,1]nonane and many of its derivatives have a marked effect on cholinergic systems in the organism [22]. Quaternary amino-derivatives of this series exhibit a curare-like activity [22]. Many derivatives of 3,9-diazabicyclononane exhibit similar properties [23]. A number of derivatives of 3-azabicyclononane have ganglion-blocking and hypotensive activities [24,25]. Derivatives of 1,5-diphenyl-3,7-diazabicyclonan-9-one behave as local anaesthetics [26]. Other pharmacological properties of 3,7-diazabicyclo[3,3,1]nonane ("bispidine") are described by Chiavarelly et al. [27]

The available literature data have been classified in this review on the basis of the type of the formal mechanism of synthesis and not on the basis of the type of heteroatoms. This treatment makes it possible to find typical methods of preparation, reveals the genetic relation between structures with different heteroatoms, and permits the most compact systematic account of the data. We may also note that Italian authors have published a review on 3,7-diaza-derivatives covering the literature up to 1968. [27] Therefore, in the discussion of bispidines we shall consider mainly the new literature, selecting from the older studies only those which are fundamentally essential for a systematic description.

2. SYNTHESIS FROM *cis*-1,3-DISUBSTITUTED HETERO-ANALOGUES OF CYCLOHEXANE

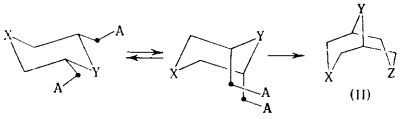
One of the commonest methods of synthesis of hetero-bicyclononanes involves the cyclisation of 1,3-disubstituted cyclohexanes and their heteroanalogues via the following mechanism:



(IV) (V) (II) (VI)

The bicyclic structure can be synthesised either by the interaction of the bifunctional compound (IV) with a suitable reagent (V) [mechanism (1a)] or via intramolecular cyclisation according to mechanism (1b). Possibly the true mechanism of the conversion of compound (IV) into (II) includes the intermediate formation of the derivative (VI). When Z = nitrogen or sulphur, the commonest procedure involves the condensation of a dihalide (IV, A = halogen), di(toluene-p-sulphonate) (IV, A = OTs), or di(methane-sulphonate) (IV, A = OMs) with an amine or sodium sulphide respectively. Although mechanism (1a) has been used to synthesise oxygen-containing compounds (II, Z = O) by the reaction of a dihalide with silver oxide[28], the commonest procedure in this case involves the intramolecular cyclisation of diols (VI, A = ZB = OH) with elimination of the elements of water[29-31].

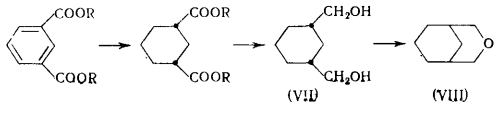
Evidently cyclisation with formation of compound (II) is possible only for *cis*-1,3-disubstituted cyclohexanes in the diaxial conformation:



(II)

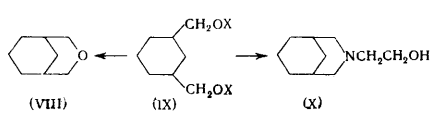
When the size of the substituent is moderate, the *cis*-isomers of 1,3-disubstituted cyclohexane usually assume the diequatorial conformation, becoming more stable in consequence than the equatorial-axial *trans*-isomers. Thus the difference between the free energies of the *cis*- and *trans*-isomers of 1,3-dimethylcyclohexane is 1.96 kcal mole^{-1} at 25°C.[32] Hence the problem of the synthesis of heterobicyclononanes reduces to the synthesis of the *cis*-isomer of a 1,3-disubstituted heteroanalogue of cyclohexane. For this purpose, one must choose either a stereoselective reaction or the mechanism must include a thermodynamically controlled stage, as a result of which the more stable *cis*-isomer predominates.

One of the commonly used reactions is catalytic hydrogenation of 1,3-bifunctional six-membered aromatic systems. Thus hydrogenation of isophthalic acid ester leads to the diol (VII), the dehydration of which yields oxabicyclononane (VIII):[29]



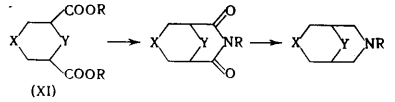
(VII) (VIII)

Catalytic hydrogenation of the ring and reduction of the methoxycarbonyl group can be carried out in stages[33]. The cyclisation has also been achieved by heating the di(methanesulphonate) (IX, X = Ms) with potassium hydroxide[33]:



(VIII) (IX) (X)

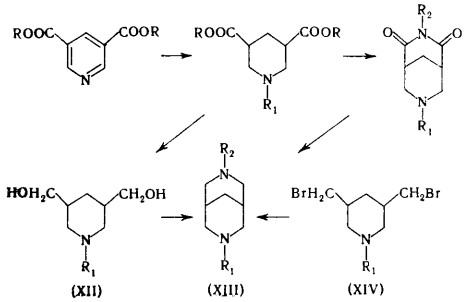
The interaction of the di(toluene-p-sulphonate) (IX, X = Ts) with ethanolamine leads to a derivative of azabicyclononane (X).[34,35] The latter is readily obtained also by the reduction of the imide of hexahydroisophthalic acid (IX, X = Y = CH_2) with lithium aluminium hydride[34]:



(XI)

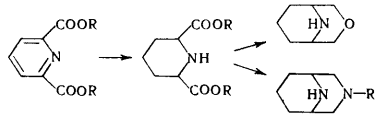
This scheme has been used to synthesise also other heteroanalogues[36-47].

The starting material for the synthesis of bispidines (XIII) may be a pyridine-3,5-dicarboxylic acid ester[12]:

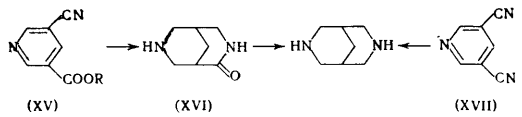


(XII) (XIII) (XIV)

Other versions of this synthesis involve the cyclisation of the dibromide (XIV)[48] or the diol (XII) in the presence of hydrogen bromide[11]. Similarly 3-oxa-9-aza[30] and 3,9-diaza-bicyclononane have been obtained from pyridine-2,6-dicarboxylic acid[46]. The same scheme has been used to synthesise 9-methyl-3,9-diaza-compounds[37]:

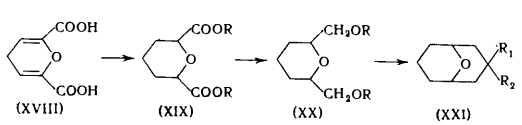


Catalytic hydrogenation of the mononitrile (XV) leads to bispidone (XVI), which is readily reduced to bispidine[49]:



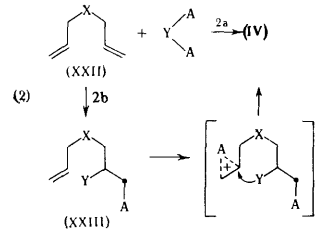
(XV) (XVI) (XVII)

Sometimes the catalytic hydrogenation and cyclisation occur in a single stage. Thus the hydrogenation of the nitrile (XVII) under severe conditions yields bispidine at once[50]. It is readily seen that the catalytic hydrogenation method is restricted mainly to benzene and pyridine derivatives, although instances of the use of other unsaturated systems are known. Thus the reduction of pyrandicarboxylic acid (XVIII) to the tetrahydro-compound (XIX, R = H) with subsequent reduction of the ester leads to the diol (XX, R = H) with the *cis*-configuration. Tosylation of the diol followed by treatment with sodiomalonic ester leads to the oxa-derivative (XXI).[51] However, we may note that 9-oxa-derivatives are more conveniently obtained from cyclo-octadiene (see below).



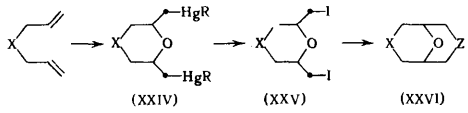
(XVIII) (XIX) (XX) (XXI)

Another general method of synthesis involves the formation of a *cis*-1,3-disubstituted cyclohexane fragment from acyclic 1,6-diene systems of type (XII) via mechanism (2):



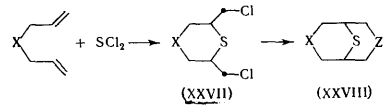
The reaction of electrophilic agents with dienes of this type can involve both double bonds [mechanism (2a)]. Another version of this process may be the addition of an electrophilic agent to one double bond with formation of the intermediate (XXIII), the functional group Y of which is capable of nucleophilic attack on the intermediate 'onium ion in the second stage of the electrophilic addition [mechanism (2b)]. Thus the second stage may be regarded as coupled addition to a multiple bond. The wide variety of electrophilic agents, the possibility of varying the heteroatom in the initial diene system, and the ease of varying the heteroatom in the last stage of the cyclisation of the 1,3-disubstituted heteroanalogue of cyclohexane make this method very convenient for the synthesis of different 3,7,9-heterobicyclononanes.

The easily available diallyl ether, diallyl sulphide, or diallylamine can be used as the diene components. The choice of the electrophilic agent is restricted by the following requirements. Firstly, it must be capable of cyclisation via two bonds and therefore the number of the usual addition products must be reduced to a minimum. Normally this condition is fulfilled by relatively weak electrophilic agents (mercury salts, sulphur dichloride). Secondly, an intermediate (XXIII) must be obtained, in which the Y group must be capable of further nucleophilic reaction or at any rate can be easily transformed into such a group. Both requirements are satisfied by the hydroxymercuration reaction. Thus hydroxymercuration of diallyl ether [52-54], diallyl sulphide [55], and diallylamine [14] leads to chloromercuri-derivatives of tetrahydropyrans of type (XXIV):



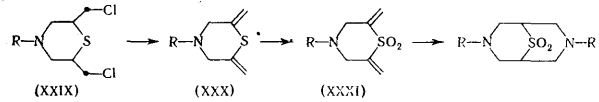
In most cases the reaction is stereoselective and leads to *cis*-isomers, although the presence of *trans*-isomers has also been established in a number of cases [53-55]. Treatment of mercuri-derivatives with iodine converts them smoothly into di-iodides (XXV). Cyclisation of the di-iodide (XXV, X = O) with silver oxide yields 3,7,9-trioxabicyclononane ("Stuehr's ether") [28]. Similarly treatment of compounds of type (XXV) with amines yielded 7-phenyl-3,9-dioxa-7-azabicyclononene (XXVI, X = O, Z = NPh) [53] and a substituted 9-oxabispidine (XXVI, X = NR_1, Z = NR_2). [14] Condensation of compounds of type (XXV) with sodium sulphide gave 9-oxa-3,7-dithia- [55] and 3,9-dioxa-7-thia-bicyclononanes [56] (XXVI, X = Z = S and X = O, Z = S respectively). It is interesting that bis-iodomethyloxathiane (XXV, X = S) reacts smoothly with sodium selenide to form 9-oxa-3-thia-7-selenabicyclononane (XXVI, X = S, Z = Se). [56]

Another widely used reaction involves the addition of sulphur dichloride. The addition of this reagent to diallyl ether [57], diallyl sulphide [57], and diallylamine [58] proceeds with formation of dichlorides of type (XXVII)

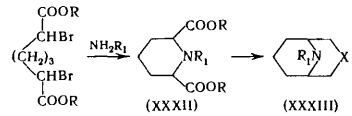


3-Oxa-7-9-dithia-, 3,7,9-trithia-, and 3-phenyl-7,9-dithia-3-azabicyclononanes were obtained by this procedure [56].

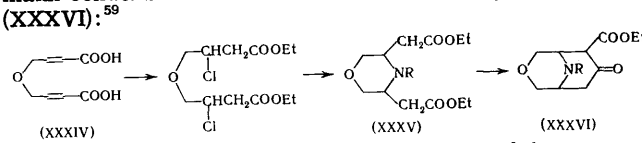
The sulphides formed can be oxidised to the sulphoxides or sulphones [57]. In many cases this permits an alternative type of cyclisation in the last stage, which can be used when the configuration of compound (XXVII) is unfavourable. For example, treatment of the bischloromethyl derivative (XXIX) with alkali yielded the diene (XXX), which was further oxidised to the sulphone (XXXI). The presence of the unsaturated sulphone fragment makes it possible to carry out nucleophilic addition to multiple bonds and thus obtain the sulphone of 3,7-disubstituted 9-thia-3,7-diazabicyclononane [58]:



Another typical reaction leading to bifunctional heteroanalogues of cyclohexane is the cyclisation of 1,5-dihalogeno-derivatives. Thus the reaction of the 2,6-dibromomopimelic ester with amines yields piperidines (XXXII), which have been used to synthesise 3,9-diaza- (XXXIII, X = NR_2) [43] and 3-oxa-9-aza-bicyclononanes (XXXIII, X = O): [31]

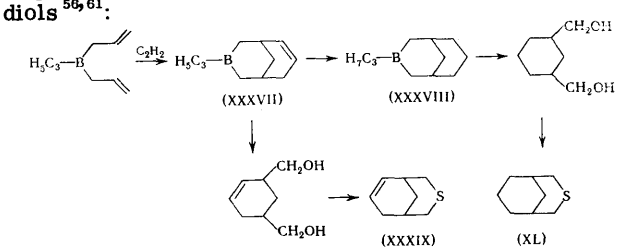


The addition of hydrogen chloride to the unsaturated acid (XXXIV) and subsequent cyclisation give rise to morpholine (XXXV). The latter was subjected to Dieckmann condensation with formation of the bicyclic ketoacid (XXXVI): [59]

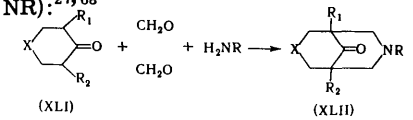


The synthesis of *cis*-1,3-disubstituted cyclohexanes from borabicyclic compounds is extremely interesting and promising. Triallylboron condenses with acetylene to give a high yield of borabicyclononene (XXXVII). [60] The latter can be converted into the saturated analogue (XXXVIII). In turn, these compounds can also be converted into *cis*-diols by the usual hydroboration method.

The 3-thiabicyclononene (XXXIX) and 3-thiabicyclononane (XL) have been obtained by the reaction of sodium sulphide with the di(toluene-*p*-sulphonates) of these diols [56,61]:

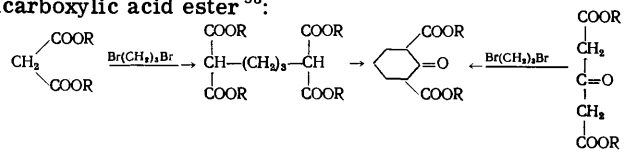


One of the typical reactions employed in the synthesis of bicyclononane structures is the Mannich condensation. With the cyclohexanones (XLI, X = CH_2), the reaction leads to 3-azabicyclononanes (XLII, X = CH_2).[38,62-67] The interaction of piperidinones (XLI, X = NR) with formaldehyde and amines results in the formation of bispidines (XLII, X = NR):[27,68]

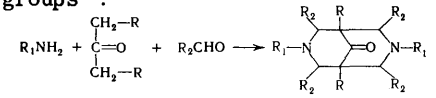


(XLI) (XLII)

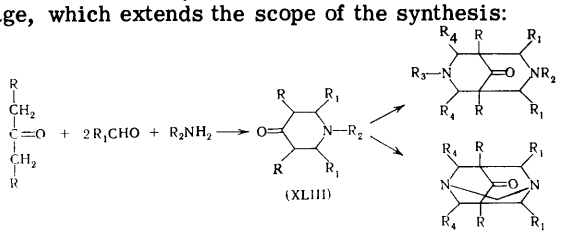
Usually R_1 and R_2 are ethoxycarbonyl groups[62,63,67,68], although the reaction takes place also when $R_1 = R_2 = H$.[65] The carboxy-groups in the aminoketone (XLII, $R_1 = R_2$ = COOH) can be readily removed by acid hydrolysis[38,63]. The corresponding diethoxycarbonylcyclohexanone can be obtained from β-dicarbonyl compounds[38] or from acetonedicarboxylic acid ester[38]:



Bispidines can also be synthesised from ketones with two methylene groups[27]:



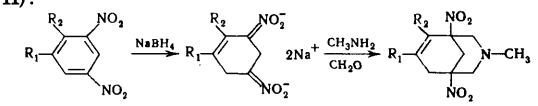
The method permits an extensive variation of the substituent, since the reaction can be carried out in stages with isolation of the intermediate monocyclic compound (XLIII). Then another aldehyde can be employed in the second stage, which extends the scope of the synthesis:



(XLIII) (XLIV)

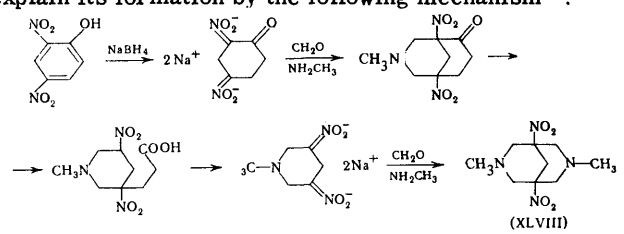
In many cases the reaction product is a compound of type (XLIV) with an adamantane structure, which can be reconverted into a bicyclic compound[69-72].

An interesting method for the synthesis of 3-azabicyclononanes is based on the use of *m*-dinitrobenzenes. The reduction of the latter leads to compounds (XLVI), the Mannich condensation of which yields the aza-derivatives (XLVII):[73-75]



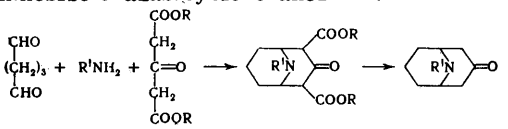
(XLV) (XLVI) (XLVII)

It is interesting that the dinitrophenol (XLV, R_1 = H, R_2 = OH) gives rise under these conditions to an anomalous product—the dinitrobispidine (XLVIII). The authors explain its formation by the following mechanism[75]:

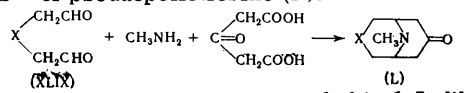


(XLVIII)

The Robinson–Schopf condensation can be used extensively to synthesise 9-azabicyclononanes[76,77]:

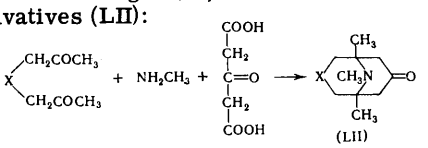


We may note that the synthesis of N-methyl-9-azabicyclo[3,3,1]nonan-3-one ("pseudopelletierine") plays an important role in the determination of the structure of cyclo-octatetraene[78,79]. This reaction makes it possible to vary the substituents, is convenient for preparative purposes, and usually takes place with a high yield[13,80-87]. It can be extended to glutaraldehydes with functional substituents, for example 3-phenyl[83] or 3-ethoxy-derivatives[13]. Heteroanalogues of glutaraldehyde (XLIX) have also been used in this reaction, which permitted the synthesis of thia-,[88,89] oxa-,[89] selena-,[88] and *N*-methylaza-analogues[88] of pseudopelletierine (L):



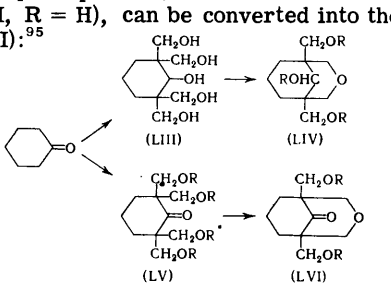
(XLIX) (L)

Recently this condensation was extended to 1,5-diketones[90]. Thus the condensation of heptane-2,6-dione (LI, X = CH_2) and its 4-thia-analogue (LI, X = S) leads smoothly to the aza-derivatives (LII):



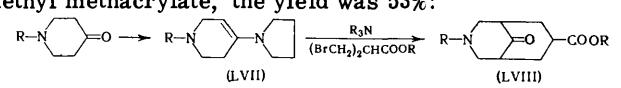
(LII)

As early as 1891, Tollens showed that the condensation of aliphatic aldehydes and ketones with formaldehyde in the presence of calcium oxide yields polyhydric alcohols[91]. Under these conditions, cyclohexanone forms the pentahydric alcohol (LIII),[92] which is dehydrated by hydrogen chloride to form the cyclic ether (LIV, R = H).[92,93] Treatment with acetic acid yields the acetate (LIV, R = Ac).[94] When the condensation is carried out under milder conditions, the carbonyl group is not involved and the tetra(toluene-*p*-sulphonate) obtained from the tetrahydric alcohol (LVI, R = H), can be converted into the cyclic product (LVI):[95]



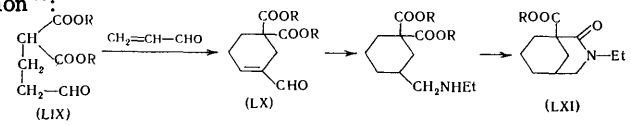
(LIII) (LIV) (LV) (LVI)

In synthetic studies on steroids, it was found that the concentration of unsaturated ketones and cyclic ketones and diketones can proceed via the intermediate formation of compounds with the bicyclo[3,3,1]nonane skeleton[96]. Similarly cyclisation of enamines of cyclic ketones with unsaturated carbonyl compounds or β-halogenocarbonyl compounds likewise constitutes a general method of synthesising bicyclononanes[15]. These reactions can be achieved also when the initial compounds contain heteroatoms. Thus the aza-compound (LVIII) was obtained in 80% yield from the enamine (LVII) by condensation with $\beta\beta$-dibromoisobutyrate[97]. In the reaction with β-bromomethyl methacrylate, the yield was 53%:[97]



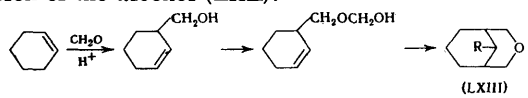
(LVII) (LVIII)

The reaction with acrolein proceeds similarly [98]. An example of the condensation of an unsaturated aldehyde with an aliphatic carbonyl compound leading to a cyclic product is the interaction of the diethoxycarbonylaldehyde (LIX) with acrolein. The resulting unsaturated aldehyde (LX) cyclises to the lactam (LXI) after reductive amination [99]:



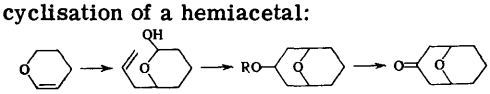
(LIX) (LX) (LXI)

The reaction of formaldehyde with cyclic olefins (the Prins reaction) has found some application in the synthesis of oxygen-containing bicyclononanes. According to Blomquist and Wolinsky [100] and Dolby and Schwarz [101], the formation of substituted 3-oxabicyclononanes from cyclohexane is stereoselective and proceeds via the intermediate formation of the alcohol (LXII):



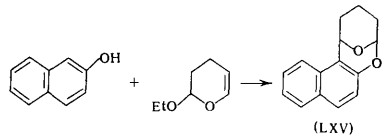
(LXII) (LXIII)

Various substituted oxabicyclononanes of type (LXIII) have been obtained by means of this reaction [100-103]. When the condensation is carried out in the presence of hydrochloric acid, the main product is the *anti*-9-chloro-derivative (LXIII, R = Cl). [104] This chloride is readily reduced to 3-oxabicyclo[3,3,1]nonane [104]. 9-Oxabicyclononane (LXIV) was obtained from dihydropyran by a procedure [105] involving the cyclisation of a hemiacetal:



(LXIV)

Here it is also appropriate to describe the formation of the tricyclic compound (LXV) with the 2,9-dioxabicyclo[3,3,1]-nonane moiety from ethoxydihydropyran and β-naphthol [106]:

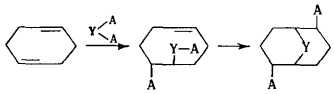


(LXV)

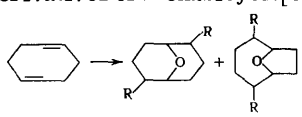
3. SYNTHESIS FROM CYCLO-OCTANE DERIVATIVES

One of the versions of the synthesis of the above bicyclic compounds under consideration involves the cyclisation of compounds which already contain an eight-membered ring in their structure. Such cyclisation can be achieved by electrophilic addition to cyclo-octa-1,5-diene via the following procedure:

(3)



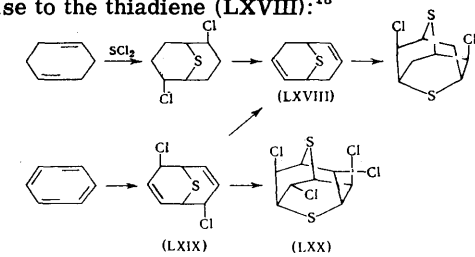
Evidently all the remarks made above concerning the addition to the 1,5-diene system are valid also for this type of addition. Indeed the hydroxymercuration reaction readily yields derivatives of 9-oxabicyclo[3,3,1]nonane [107-110]:



(LXVI) (LXVII)

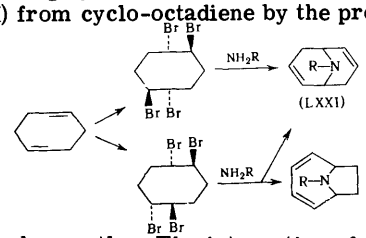
A detailed study of this reaction showed that, together with compounds having the structure of bicyclo[3,3,1]nonane, derivatives of bicyclo[4,2,1]nonane (LXVII) are also formed [108,109]. Their proportions depend sometimes on the reaction conditions, which makes it possible to drive the process towards the preferential formation of compounds of the bicyclo[3,3,1]nonane series (LXVI). [109]

The reaction with sulphur dichloride [111,112] and Se_2Cl_2 (Lautenschlaeger [16]) takes place similarly. It is interesting that cyclo-octatetrane can be introduced into the reaction with SCl_2. [18,113] The reaction can be stopped at the stage of the diene (LXIX), the subsequent interaction of which with a second mole of SCl_2 yields dithia-adamantane (LXX). The reduction of the dichloride (LXIX) gives rise to the thiadiene (LXVIII):[18]



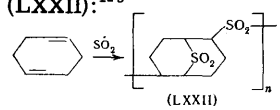
(LXVIII) (LXIX) (LXX)

An interesting synthesis of 9-azabicyclononane-2,6-diene (LXXI) from cyclo-octadiene by the procedure [114]



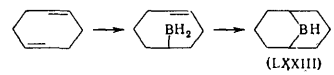
(LXXI)

was described recently. The interaction of cyclo-octa-1,5-diene with sulphur dioxide in the presence of radical initiators takes place in an interesting way. The reaction product is a polymer, the structural unit of which is a bicyclic sulphone (LXXII):[115]



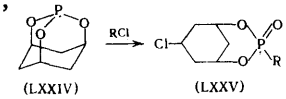
(LXXII)

Evidently the range of electrophilic agents which react according to this mechanism can be extended. For example, it is known that diborane reacts with cyclo-octadiene to form 9-borabicyclononane (LXXIII) [116]:



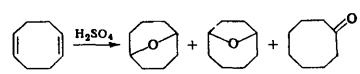
(LXXIII)

Probably one can select conditions for the synthesis of other organic derivatives of the elements using suitable selenium, phosphorus, etc. compounds as electrophilic agents. We may note that bicyclic phosphonates of type (LXXV), which are formed by the Arbuzov reaction between the heteroadamantane (LXXIV) and an alkyl chloride [117],

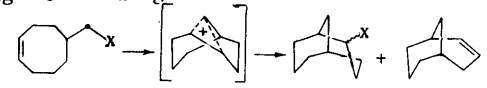


(LXXIV) (LXXV)

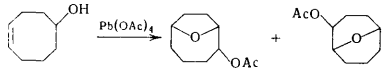
have been described. The interaction of cyclo-octadiene with sulphuric acid can also be included among reactions of this type [118]:



A second set of reactions includes transannular processes in eight-membered rings, for example those involving the following mechanism:

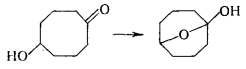


We shall not consider the mechanism of these reactions, which has been dealt with fairly thoroughly in the literature [119–122], and shall discuss the synthetic aspect of the problem. These reactions are usually employed to synthesise 9-oxa-derivatives. Thus cyclisation of the unsaturated alcohol (LXXVI) lead tetra-acetate yields smoothly the bicyclic compounds (LXXVII) and (LXXVIII):[123]

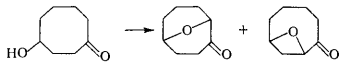


(LXXVI) (LXXVII) (LXXVIII)

According to Cope et al. [108], 5-hydroxycyclo-octanone exists in the hemiacetal form:

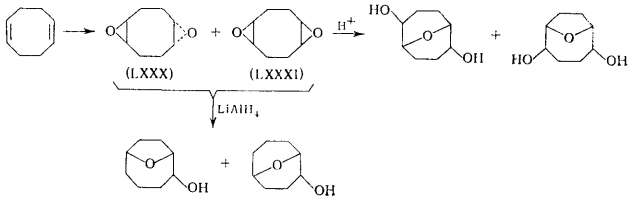


A transannular reaction was observed when the hydroxyketone (LXXIX) was brominated and the crude product was treated with potassium hydroxide [108]:



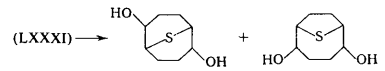
(LXXIX)

The formation of derivatives of isomeric bicyclononanes as a result of ring opening in the epoxides (LXXX) and (LXXXI) [124] belongs to reactions of the same type:

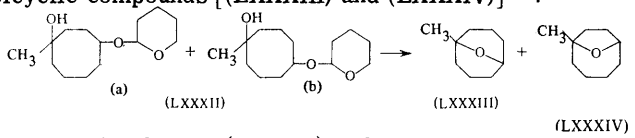


(LXXX) (LXXXI)

When the *cis*-diepoxide (LXXXI) is treated with sodium sulphide, a 9-thia-derivative is formed [124]:

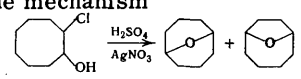


On treatment with acid, a mixture of cyclic tetrahydropyranyl ethers (LXXXII, a and b) also give a mixture of bicyclic compounds [(LXXXIII) and (LXXXIV)] [125]:



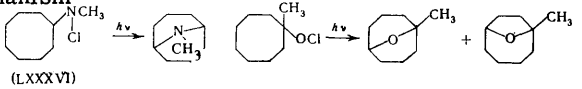
(a) (LXXXII) (b) (LXXXIII) (LXXXIV)

The chlorohydrin (LXXXV) undergoes transannular cyclisation via the mechanism [126]



(LXXXV)

Chloroamines are known to be cyclised under the influence of sulphuric acid or on heating into cyclic amines [127]. Similarly irradiation of the chloroamine (LXXXVI) is accompanied by transannular cyclisation according to the mechanism [128]

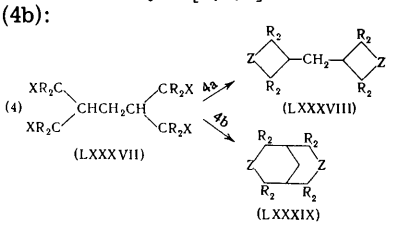


(LXXXVI)

A similar transannular rearrangement is observed for 1-methylcyclo-octyl hypochlorite [125]. There is no doubt that photochemical transannular cyclisation is extremely promising.

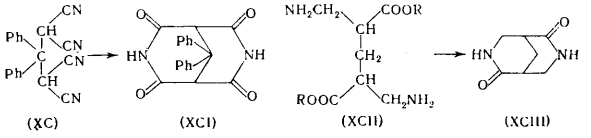
4. SYNTHESIS FROM 1,1,3,3-TETRASUBSTITUTED PROPANES

Symmetrical 1,1,3,3-tetrasubstituted propanes (LXXXVII) can be converted into bicyclo[3,3,1]nonanes (LXXXIX) via mechanism (4b):



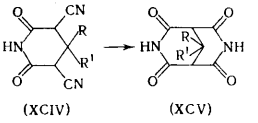
(LXXXVII) (LXXXVIII) (LXXXIX)

However, the cyclisation can also follow the alternative mechanism (4a) with formation of cyclobutane derivatives (LXXXVIII). The relative contributions by these two mechanisms depend on the type of reaction. Thus the cyclisation of the tetra(toluene-*p*-sulphonate) of 2,4-di-(hydroxymethyl)pentane-1,5-diol (LXXXVII, R = H, X = OTs) by reaction with disodiomalonic ester proceeds via mechanism (4a) with formation of the tetraester [(LXXXVIII), Z = C(COOR')$_2$]. [129] On the other hand, acid hydrolysis of the tetranitrile (XC) leads to the diimide (XCI), which has a bicyclononane skeleton [130]:



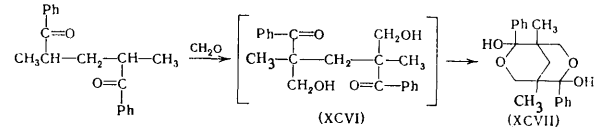
(XC) (XCI) (XCII) (XCIII)

The formation of the dilactam (XCIII) from the bis-aminoester (XCII) proceeds similarly [131]. In these cases the cyclisation can probably be carried out in stages. At any rate, acid hydrolysis of the dinitrile (XCIV) also yields compound (XCV) with a bispidine structure [132–134]:



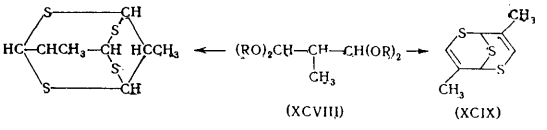
(XCIV) (XCV)

The cyclisation of the intermediate ketol (XCVI), leading to the formation of a derivative of 3,7-dioxabicyclononanediol (XCVII), takes place in a similar manner [135]:



(XCVI) (XCVII)

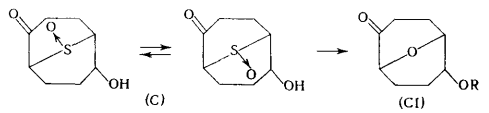
In the synthesis of tetrathia-adamantane from the diacetal (XCVIII) and hydrogen sulphide, the diene (XCIX) is formed as a side product [136]:



(XCVIII) (XCIX)

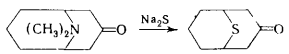
5. SPECIAL METHODS OF SYNTHESIS

In conclusion we shall describe several unique reactions involving changes in the heteroatoms in the bicyclic system under consideration. Thus the β-ketosulphoxide (C) is converted into the 9-oxa-derivative (CI) on irradiation [137]:



(C) (CI)

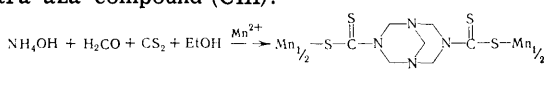
The reaction of pseudopelletierine methiodide (CII) with sodium sulphide, which leads to a smooth replacement of the heteroatom, is very interesting [138,139]:



(CII)

It is possible to put forward several versions of the mechanism of this reaction, in particular an elimination–addition mechanism; however, it would be interesting to make an experimental study of this problem.

Examples of polycondensations leading to structures with a bicyclononane skeleton are known. For example, the reaction of formaldehyde with ammonia and carbon bisulphide in the presence of manganese(II) sulphate yields the tetra-aza-compound (CIII):[140]



(CIII)

The mechanism of this condensation is not known in detail and it maybe that the reaction involves one of the mechanisms described above.

---o0o---

The foregoing data show that synthetic methods leading to heteroanalogues of bicyclo[3,3,1]nonane are fairly varied and include many procedures of preparative organic chemistry. It is quite evident that in future one may expect an increase in the number of studies in this field in view of the practical importance of compounds of this series and the enormous advances in the development of synthetic methods in general. The development of methods in the chemistry of organic derivatives of the elements gives rise to the self-evident possibility of extending the range of heteroatoms in this bicyclic system. The appearance of many new reactions involving coupled addition to a multiple bond greatly extends the scope of the heterocyclisation of diene systems. Finally, the new photochemical reactions which have been developed are also promising for the synthesis of heterobicyclononanes.

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Laboratory of Heterocyclic Compounds, Faculty of Chemistry, Moscow State University

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Carbonylation of Polyunsaturated Hydrocarbons and of Saturated and Unsaturated Alcohols and Halogeno-derivatives

Ya.T.Eidus, A.L.Lapidus, K.V.Puzitskii, and B.K.Nefedov

A survey is made of the catalytic carbonylation of various di- and poly-unsaturated hydrocarbons, alcohols and halogeno-derivatives by carbon monoxide in the presence of complexes of Group VIII metals and acid catalysts. A list of 200 references is included.

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I. INTRODUCTION

Active investigations of carbonylation with carbon monoxide have been made not only on unsaturated hydrocarbons containing one multiple bond [1] but also on polyunsaturated hydrocarbons together with various alcohols and halogeno-derivatives. These reactions take place under conditions of homogeneous catalysis in the presence of catalysts based on Group VIII metals (predominantly complexes). The carbonylation of saturated alcohols and of polyenes with well separated double bonds occurs under conditions of acid catalysis. The survey covers these reactions except for those involving hydroformylation, which has been widely discussed in the literature.

II. CARBONYLATION OF DI- AND POLY-UNSATURATED HYDROCARBONS

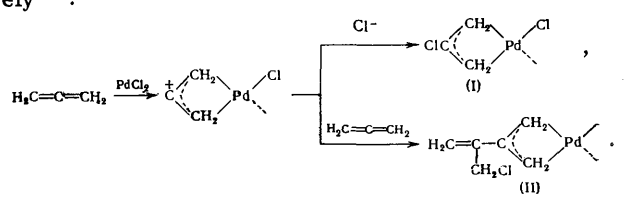
1. Reactions of the presence of Catalysts based on Group VIII Metals

(*a*) Enynes and Diynes

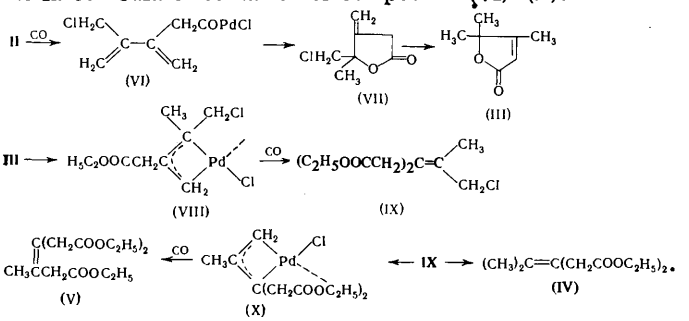
Butenyne is more difficult to carbonylate by means of tetracarbonylnickel than are hydrocarbons containing only a triple bond. The chief product is the cyclic dimer of 2-methylenebut-3-enoic acid [2]. The reaction is accelerated by the addition of pyridine [3,4]. It has not proved possible to carbonylate butadiyne [5].

(*b*) Dienes and polyenes

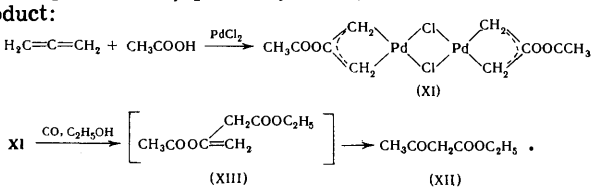
With palladium dichloride allene forms the complexes (I) and (II) in benzene and methanolic solution respectively [6-8]:



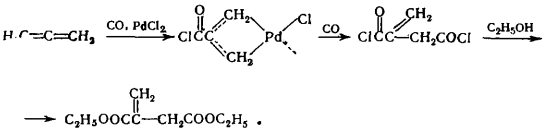
The formation of derivatives of $\beta\gamma$-unsaturated acids from π-allyl complexes of palladium has been investigated [9-12]. Complex (I) in an alcoholic medium at 100°C under carbon monoxide pressures of 100–110 atm yields the 3-chlorobut-3-enoic ester [13]; and complex (II) forms the γ-lactone of 4-hydroxy-3,4-dimethylpent-2-enoic acid (III), the β-isopropylideneglutaric diester (IV), and a triester (V), with the intermediate formation of compounds (VI)–(X):



The carbonylation of allene in the presence of palladium dichloride and the carboxylate ion (in a solution of sodium chloropalladate and acetate in acetic acid) at room temperature gives the di-μ-chlorobis-(2-acetoxy-π-allylpalladium) complex (XI); and the latter in benzene at 100°C and a carbon monoxide pressure of 100 atm forms the compound (XII), probably with (XIII) as intermediate product:



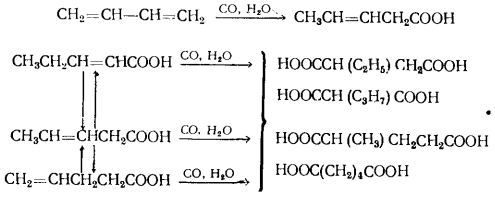
Carbon monoxide acts on allene in ethanol to give a low yield of itaconic ester [13]:



In the presence of small quantities of ruthenium nonacarbonyl or trichloride in methanol at 150°C and a carbon monoxide pressure of 900 atm allene is converted into methyl methacrylate (18%) and dimethyl $\alpha\alpha$-dimethyl-α'-methyleneglutarate (23%), but on the addition of pyridine the products are methyl methacrylate and methyl 1,3,4-trimethylcyclohex-3-enecarboxylate. In an aqueous medium methacrylic acid or the lactones of 3- and

4-hydroxy-1,3,4-trimethylcyclohexanecarboxylic acids are formed (at 700–1000 atm) [14].

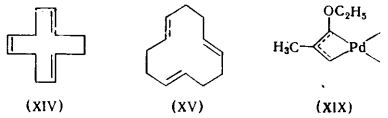
The carbonylation of butadiene gives a mixture of dicarboxylic acids, with the intermediate formation of vinylcyclohexene [15]. Rudkovskii and his coworkers [16–21] obtained from butadiene, carbon monoxide, and water in the presence of bistetracarbonylcobalt at 160–200°C and 250 atm pent-3-enoic acid and products of the carbonylation of this acid (and its isomers)—unsaturated C_6 dicarboxylic acids—contaminated with valeric acid:



This process is accomplished by the addition of pyridine, which reacts with unsaturated acyl carbonyls, thereby preventing side-reactions [22,23]. The yield of reaction products was raised by using 4,4′-bipyridyl instead of 2,2′-bipyridyl as solvent [24,25].

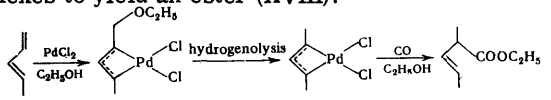
Cobalt carbonyl is the best catalyst for the reaction in pyridine solution. Rhodium and iridium carbonyls are less active and less selective. Iron carbonyl has little activity, and nickel carbonyl is completely inactive. The selectivity (with respect to pent-3-enoic acid) falls in the sequence cobalt > rhodium > iridium [20]. Addition of the elements of formic acid H–COOH can occur also at the 1,2-positions with the formation of pent-4-enoic and 2-methylbut-3-enoic acids. The latter isomerises to 2-methylbut-2-enoic and α-methylenebutyric acids [16]. The rates of formation of pent-3-enoic acid (yield up to 95%) and C_6 tricarboxylic acids (up to 65%) are directly proportional to the concentrations of catalyst and butadiene, decrease with increase in the concentration of water, and pass through a maximum with increase in the pyridine concentration and the carbon monoxide pressure [21]. The reactivity of dienes diminishes in the sequence—buta-1,3-diene, isoprene > hexa-1,5-diene > penta-1,3-diene, hexa-2,4-diene > 2,3-dimethylbuta-1,3-diene. The diene undergoes rapid *cis–trans* isomerisation under the reaction conditions, but its geometrical configuration has no significant effect on the reaction velocity. Penta-1,3-diene undergoes secondary hydrogenation to pentane [17]. In the presence of a palladium catalyst, e.g. $[Pd((C_6H_5)_3P)_2]\cdot Cl_2/HCl$, the carbonylation of butadiene takes place at ~120°C with the formation of pent-2-enoic acid [26–28]. In the absence of pyridine, rhodium catalysts promote the formation of unsaturated esters from conjugated dienes [29].

Carbon monoxide acts on the *cis–trans–trans* and *trans–trans–trans* forms of cyclododeca-1,5,9-triene (XIV and XV) in the presence of a finely dispersed metal, salt, or carbonyl (nickel or cobalt) to give cyclododecanecarboxylic acid or (in methanol) its ester in 60% yield, together with cyclododecadiene, cyclododecene, and cyclododecylmethanol [30].



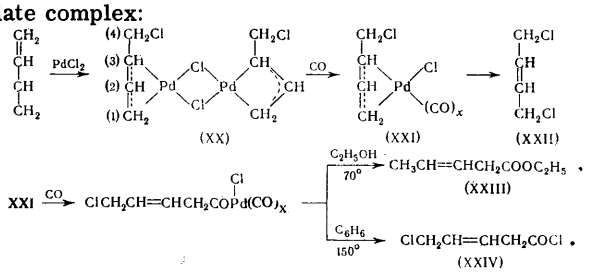
(XIV) (XV) (XIX)

The carbonylation of penta-1,3-diene in ethanolic solution in the presence of small quantities of palladium dichloride at 110°C and 120 atm depends on intermediate formation of ethoxy-π-allyl (XVI) and symmetrical (XVII) complexes to yield an ester (XVIII):[31]



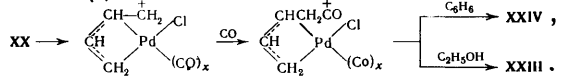
(XVI) (XVII) (XVIII)

Intermediate formation of the complex (XVI) is based on results [32] indicating that the carbonylation of butadiene and isoprene involves intermediate formation of the complex (XIX), which undergoes hydrogenolysis, as is indicated by the production of pent-3-enoic and 4-methylpent-3-enoic esters. In the presence of palladium dichloride various derivatives of unsaturated acids are formed depending on the reaction conditions, in conformity with two modes of attack by carbon monoxide on the intermediate complex:

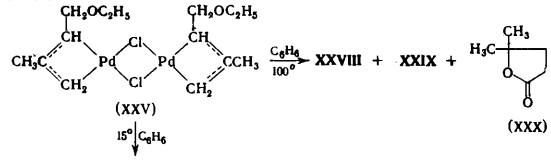


(XX) (XXI) (XXII) (XXIII) (XXIV)

The relative yields of (XXII) and (XXIV) are 3 : 2 in benzene and 1 : 2 in ethanol. Compound (XXIII) is formed by the attack of carbon monoxide on the $C_{(1)}$ atom followed by hydrogenolysis and detachment of chlorine from $C_{(4)}$. Attack by carbon monoxide on $C_{(4)}$ with hydrogenolysis at $C_{(1)}$ is also possible. Product (XXIV) can be produced by the attack of carbon monoxide on $C_{(4)}$ with the appearance of an intermediate carbonium ion and by the attack of chlorine on $C_{(1)}$.[32]

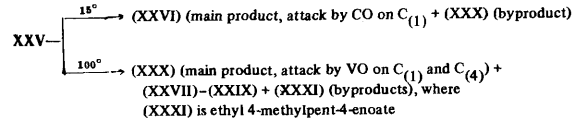


In the reaction with isoprene, attack by carbon monoxide at $C_{(1)}$ and $C_{(4)}$ atoms leads to the formation of different products:

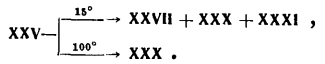


(XXV) (XXVI) (XXVII) (XXVIII) (XXIX) (XXX)

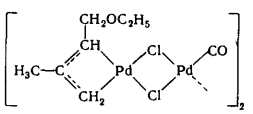
The 4-ethoxyl in the complex (XXV) is readily eliminated, as is chlorine from (XX), to form a carbonium ion. In benzene a mixture of acid chlorides and esters is formed, mainly as a result of attack by carbon monoxide on $C_{(1)}$ at room temperature and on this atom and $C_{(4)}$ at higher temperatures. At room temperature (XXVI) is the main product, while (XXVII) and (XXVIII) are side-products; at 100°C the main product is (XXVIII), with (XXIX) and (XXX) (γγ-dimethylbutyrolactone) as secondary products. In ethanol the reaction is



When hydrogen chloride is introduced into the reaction mixture at room temperature, attack by carbon monoxide on $C_{(4)}$ is accompanied by hydrogenolysis:



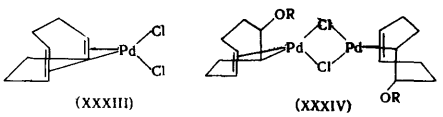
In benzene and alcohol at room temperature a new complex



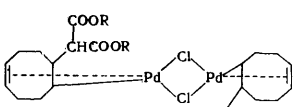
(XXXII)

is formed[33].

Metallic palladium is active only in the presence of hydrogen chloride. The reaction of cyclo-octa-1,5-diene involves intermediate formation of the complex (XXXIII), which could be isolated. The products were a monoester and a mixture of diesters, with the possibility of selective formation of the monoester. Carbonylation of (XXXIII) yields cyclo-oct-4-enecarboxylic and cyclo-octane-1,4- and -1,5-dicarboxylic esters. The bridged dinuclear complex (XXXIV), obtained by the action of sodium carbonate on (XXXIII) in alcohol[34], is converted by carbon monoxide in benzene at 60°C into 8-methoxycyclo-oct-4-enecarboxylic ester[35]. Cyclo-octa-1,3-diene gives a low yield of cyclo-oct-2-enecarboxylic ester. When (XXXIII) is treated with excess of ethyl malonate in the presence of sodium carbonate, the complex (XXXV) is obtained[36]. Cyclododeca-1,5,9-triene forms mono- and di-esters without ring-opening. Triesters have not been detected[37].



(XXXIII) (XXXIV)

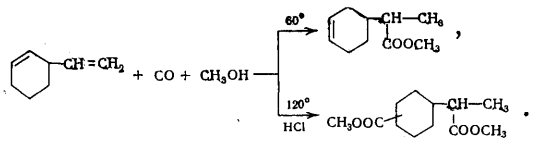


(XXXV)

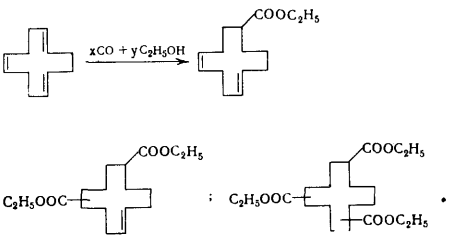
Cyclic ketones are obtained in the presence of bistetracarbonylcobalt at 165°C and a carbon monoxide pressure of 70 atm: hexa-1,5-diene yields 2,5-dimethylcyclopentanone (35%) and 2,5-dimethylcyclopent-2-enone (6%), penta-1,4-diene gives 2-methylcyclopentanone, and hepta-1,6-diene forms 2-ethyl-5-methylcyclopentanone[38].

Halides and chelate compounds of Group VIII metals, in particular ruthenium(III) acetylacetonate, catalyse the reactions of dienes with carbon monoxide and water in pyridine to form saturated monohydric alcohols. Butadiene yields pentanol and isopentanol, and hexa-1,5-diene gives heptan-1-ol, heptan-1-al, and dihexenyl ketone[39,40].

Complex compounds of palladium, platinum, and nickel with such ligands as chlorine, bromine, iodine, tertiary amines, arsines, phosphines, organic sulphides, sulphones, or phosphates in excess of alcohol are active catalysts for the carbonylation of conjugated dienes in alcoholic or phenolic medium at 200°C and carbon monoxide pressures up to 2000 atm to form esters[41]. Unstable polyenes are carbonylated in the presence of complexes of general formula PdL_mX_n, where L is a ligand (e.g. phosphine, nitryl, amine, alkene), X is an acid radical, and $m + n = 3-4$. The greatest catalytic activity is observed when $X = Cl^-$ and Br^-. These complexes exhibit catalytic activity even at concentrations of 0.05% and below at 50–140°C and 300–700 atm[42]. The reaction of vinylcyclohexene catalysed by palladium complexes is represented by the scheme[42]



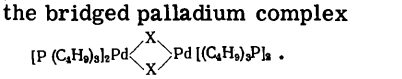
The carbonylation of several polyenes has been accomplished almost without side-reactions. Cyclododeca-1,5,9-triene forms mono-, di-, and tri-esters in up to 90% yield based on the triene that has reacted[37,42]:



The reaction is used for the industrial synthesis of trideca-1,3-lactam[42,43]. The di-μ-chlorodi-π-but-2-enyldipalladium complex is converted by carbonylation into pent-3-enoic acid[44].

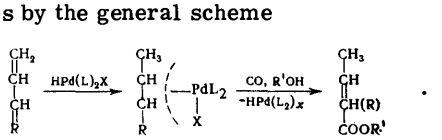
Carbon monoxide acts on butadiene in the presence of rhodium carbonyls and hydrogen chloride to give low yields of α-methylbutyrolactone and 1,3-dichlorobutane[45], but in the presence of rhodium carbonyls[46] or palladium dichloride[32,47] in an alcoholic medium pent-3-enoic esters are obtained. Alkenes react readily with palladium dichloride to form π-complexes or π-allyl complexes[48]. Buta-1,3-diene and palladium dichloride give 1-chloromethyl-π-allyl-palladium chloride[33]. The complex of palladium dichloride with butadiene is converted by carbon monoxide in benzene at 20°C and 50 atm into 5-chloropent-3-enoyl chloride and 1,4-dichlorobut-2-ene, but in an alcoholic medium at the same pressure and 70°C the products are ethyl pent-3-enoate and 1,4-dichlorobut-2-ene[47].

Complexes of palladium vary in their catalytic activity[49]. Sodium chloro- and bromo-palladates give only 1–2% yields of pent-3-enoic esters from butadiene at 70°C and 1000 atm, but with sodium iodopalladates yields of 35–40% are obtained. Modifying the catalyst by adding tributylphosphine enhances the catalytic activity and makes the catalyst thermally stable up to 150°C. In the case of palladium di-iodide the yield of esters is increased to 68%, but with the dichloride to 20%. The most active was the bridged palladium complex



(XXXVI)

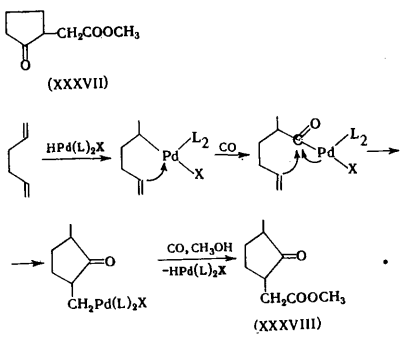
Esters of $\beta\gamma$-unsaturated acids are obtained from conjugated dienes by the general scheme



(L = ligand; X = Cl, Br, I)

Penta-1,3-diene gives methyl 2-methylpent-3-enoate (yield 34%), cyclopentadiene the cyclopent-2-enecarboxylate (70%), 2,3-dimethylbuta-1,3-diene the 3,4-dimethylpent-3-enoate (50%), and isoprene the 3-methylpent-3-enoate (15%), 4-methylpent-3-enoate (38%), and 4-methylpent-4-enoate (10%). Unconjugated dienes react more rapidly than conjugated dienes with carbon monoxide and methanol in the presence of bistributylphosphinepalladium di-iodide at 150°C and 1000 atm, to form unsaturated monoesters and saturated diesters [50]. Cycloocta-1,5-diene is converted into methyl cyclo-oct-5-enecarboxylate (45%) and the dimethyl ester of a saturated dicarboxylic acid (30%); cyclo-octa-1,3-diene gives a monoester (14%) and a diester (3%).

$\alpha\omega$-Dienes form not only unsaturated monoesters and saturated diesters but also compounds containing a ketonic group—the cyclic γ-keto-ester (XXXVII) (10%) from penta-1,4-diene, and the compound (XXXVIII) (50%) from hexa-1,5-diene:

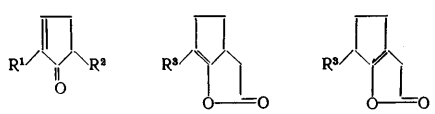


(XXXVII)

(XXXVIII)

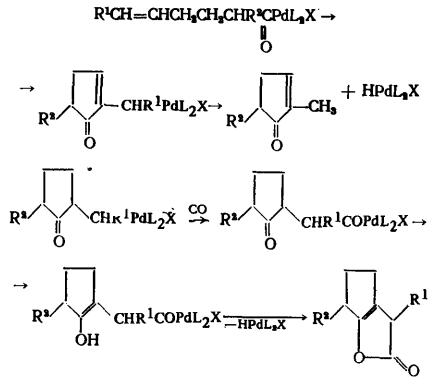
Hepta-1,6-diene gives only traces of ketonic products.

The addition of toluene-*p*-sulphonic acid to the palladium complex enables the pressure to be lowered from 1000 to 250 atm, while the reaction velocity is raised, but addition of a base, e.g. calcium acetate, lowers the rate of the reaction [50]. In the presence of 1% of bistributylphosphinepalladium di-iodide cyclo-octa-1,5-diene is converted in oxolan solution (at 150°C and 1000 atm) into bicyclo[3,3,1]non-2-en-9-one [51], but in the presence of palladium dichloride at 100°C and 100 atm the products are cyclo-oct-4-enecarboxylic and cyclo-octanedicarboxylic esters [35, 52].



(XXXIX) (XL) (XLI)

In the presence of bistributylphosphinepalladium di-iodide in oxolan at 200°C and 1000 atm $\alpha\omega$-dienes are converted into unsaturated ketones and lactones: penta-1,4-diene into 2-methylcyclopent-2-enone (XXXIX: $R^1 = CH_3$; $R^2 = H$) and a mixture of unsaturated lactones (XL, XLI: $R^3 = H$); hexa-1,5-diene into 2,5-dimethylcyclopent-2-enone (XXXIX: $R^1 = R^2 = CH_3$) and enelactones (XL, XLI: $R^3 = CH_3$); and hepta-1,6-diene into 5-ethyl-2-methylcyclopent-2-enone (XXXIX: $R^1 = C_2H_5$; $R^2 = CH_3$). Hepta-1,6-diene probably isomerises into hepta-1,5-diene before carbonylation. The addition of one carbon monoxide molecule to 1,4- and 1,5-dienes yields unsaturated cyclic ketones, but two carbon monoxide molecules give unsaturated lactones [53]:



In the presence of hydrogen iodide and nickel acetate at 270°C and a carbon monoxide pressure of 300 atm cyclo-octa-1,5-diene gives a good yield of cyclo-octanecarboxylic acid [54].

2. Reactions in the presence of Acid Catalysts

The lower dienes polymerise rapidly under the influence of strong mineral acids, and therefore are not used for the preparation of dicarboxylic acids. The latter are formed only from branched dienes in which the double bonds are separated by at least 5–8 carbon atoms. 2,5-Dimethylhexa-1,5-diene in the presence of sulphuric acid with formic acid as carbonylating agent at room temperature and atmospheric pressures gives $\alpha\alpha\alpha'\alpha'$-tetramethyladipic acid in 2–3% yield together with monocarboxylic acids (20–40%) such as 2,2,5-trimethylhexanoic acid, a dimeric C_{17} acid, and 1,2,4-trimethylcyclopentanecarboxylic acid, as well as neutral products such as esters, lactones, hydrocarbons, and 2,2,5,5-tetramethyloxolan. 2,11-Dimethyldodeca-1,11-diene forms 2,11-dimethyldodecanedicarboxylic acid (30%). [55] Cyclic polyenes—cyclododeca-1,5-diene and cyclododeca-1,5,9-triene—yield the expected di- and tri-carboxylic acids. A transannular reaction takes place with hydride migration, resulting in tricyclic systems, which combine with carbon monoxide to form acids having a carboxyl attached to the bridge carbon atom. Cyclododeca-1,5-diene forms a mixture of *cis*- and *trans*-decahydronaphthoic acids; a mixture of isomeric perhydroacenaphthenecarboxylic acids is obtained from cyclododeca-1,5,9-triene. Dienes in which the double bonds are isolated are carboxylated in the presence of the same catalyst under similar conditions to form low yields of dicarboxylic acid, and only if the double bonds are separated by 7–9 carbon atoms [56].

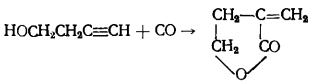
III. CARBONYLATION OF ALCOHOLS

1. Reactions in the presence of Catalysts based on Group VIII Metals

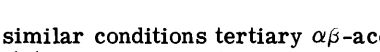
(*a*) Acetylenic alcohols

When acetylenic compounds undergo carbonylation, the carboxyl appears on a carbon atom attached to a substituent (A)—e.g. Alk, Ar, CH_2OH, CH_2CH_2OH, $CH_2CH_2CH_2OH$, $CH_3COOCHR$, $CH_2CH_2O\overline{CHO[CH_2]_3CH_2}$—that "attracts" carbon monoxide. Substituents of type B, which "repel"

carbon monoxide—e.g. H, CHROH, CR_2OH, COOH, $COOCH_3$, $COOC_2H_5$, $COCH_3$, $CH_2C(CH_3)_2OH$—promote its addition at the other carbon atom forming the triple bond. If in any compound XC : CY the substituents X and Y are both of type A, carbonylation will be rapid. When X is of type A, and Y of type B, the reaction is still quite rapid, the compound XC(COOH) : CHY being formed. If X and Y are both of type B, reaction is slow, and only after prolonged heating are unsaturated carboxylic acids formed in low yield. An exception is unsubstituted acetylene, which is carbonylated easily and smoothly [1]. Acetylenic compounds containing a primary or secondary hydroxyl give unsaturated hydroxy-acids, which under the reaction conditions often polymarise or form lactones. This route has been used to synthesise the natural antibiotic α-methylenebutyrolactone [4,5,57]:



Prop-2-ynyl alcohol reacts with carbon monoxide in ethanol in the presence of stoichiometric quantities of tetracarbonylnickel at 55°C and atmospheric pressure to give $CH_2 : C(CH_2OH)COOC_2H_5$ (58%) and $HOCH_2CH : CHCOOC_2H_5$ (11%). The methyl, n-butyl, and isobutyl esters have been prepared similarly. With catalytic quantities of the carbonyl reaction takes place at 85 to 145°C and 1.4–14 atm. A maximum pressure corresponds to a fixed reaction temperature, and exceeding this pressure by 10% brings the reaction to a halt [58]. Secondary $\alpha\beta$-acetylenic carbinols react readily with tetracarbonylnickel to form unsaturated acids:



Under similar conditions tertiary $\alpha\beta$-acetylenic carbinols, e.g. 1,1-dimethylprop-2-ynol, hardly react with stoichiometric quantities of tetracarbonylnickel [57], but in anhydrous butanol containing hydrogen chloride this carbinol gives at room temperature and atmospheric pressure a product containing $(CH_3)_2C(OH)CH : CHCOOC_4H_9$. [59] 1-Ethynylbutyl acetate in a mixture of ethanol and acetic acid reacts readily with tetracarbonylnickel at 70°C to form $CH_3CH_2CH_2CH(OCOCH_3)C(COOH) : CH_2$ (40%). [59]

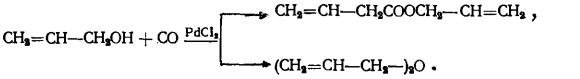
Acetylenic alcohols and glycols are carbonylated also in the presence of bistetracarbonylcobalt. In the intermediate complexes the triple bond is perpendicular to the cobalt–cobalt bond [60].

Prop-2-ynyl alcohol in methanolic hydrogen chloride, in the presence of small quantities of palladium on carbon at 100°C and a carbon monoxide pressure of 100 atm gives methyl itaconate (63%) and aconitate (10%) contaminated with methyl α-methoxymethylacrylate. Substituted prop-2-ynols react similarly [61].

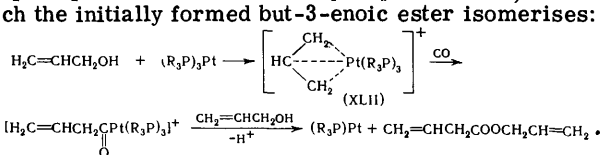
(b) Olefinic alcohols

Aliphatic 2,3- and 3,4-unsaturated alcohols and their alkylated derivatives react with carbon monoxide in the presence of bistetracarbonylcobalt or rhodium trichloride in benzene at 200–250°C and 300 atm to form γ- or δ-lactones. 2,2-Disubstituted primary alcohols give the highest yield of lactones. Primary and secondary 2,3- and 3,4-unsaturated alcohols isomerise under the reaction conditions into carbonyl compounds, the aldehydes condensing by the Tishchenko reaction. The carbonylation of tertiary 2,3- and 3,4-unsaturated alcohols is a slow reaction accompanied by dehydration. The reaction is slower in the presence of hydrogen tetracarbonylcobaltate than with bistetracarbonylcobalt [62]. Allyl alcohol gives a 60% yield of γ-butyrolactone with the latter catalyst at carbon monoxide pressures of 100–300 atm in the presence of 6–10% of hydrogen at 100–170°C. The addition of pyridine accelerates the reaction, and the use of acetonitrile and its derivatives as solvents tends to increase the rate and enhance the selectivity [63–65].

A feature of the use of palladium catalysts in the carbonylation of allyl alcohols is that the double bond may be preserved with the formation of an ester of a β-unsaturated acid [42,66]. Ethyl esters of $\beta\gamma$-unsaturated carboxylic acids are obtained from allyl alcohols in ethanol in the presence of palladium dichloride at 80–120°C and 100 atm. In the absence of a solvent the reaction is



Under the same conditions substituted allyl alcohols, e.g. but-2-enol and but-3-enol, are converted into the same product, ethyl pent-3-enoate [67]. Allyl alcohol reacts with carbon monoxide in the presence of tristri-*p*-fluorophenylphosphineplatinum to form mainly allyl crotonate, into which the initially formed but-3-enoic ester isomerises:



The π-allyl complex (XLII) is formed at 1000 atm and 200°C from allyl alcohol and a catalyst [68].

The interaction of allylic alcohols with carbon monoxide in the presence of acetylene, alcohol, tetracarbonylnickel, and hydrogen chloride yields dienoic acids with intermediate formation of allyl halides [69,70].

(c) Saturated alcohols

The earlier investigations on the carbonylation of saturated alcohols using catalysts based on Group VIII metals have been reviewed previously [71]. The carbonylation of methanol to acetic acid $CH_3OH + CO \rightarrow CH_3COOH$ has now acquired great practical importance, the most effective catalyst being cobalt acetate modified with potassium iodide. The reaction is conducted with the addition of 0.1% of the catalyst at temperatures of 220–260°C and pressures above 300 atm with 30–70 mole % of water in the methanol [72,73]. The conversion of methanol into acid is 50–80% with a constant of 40–60% of acetic acid in the reaction products. Methyl acetate is formed as an intermediate [72], the rate constant is proportional to $[CO]^2$, and its (Arrhenius) temperature dependence is non-linear [74]. The reaction has also been conducted as a continuous process at 200°C and 400 atm with an initial mixture comprising (mole %) 47.5 CH_3OH + 50.0 H_2O + 2.5 CH_3COOH and a conversion of methanol of 60.5% [75] The activity of the catalyst is adversely affected by replacing potassium iodide by iodine [76]. It has been shown spectroscopically that, in the presence of excess of iodide ions, most of the cobalt(II) forms the tetrahedral complex ion $[CoI_n(OCOCH_3)_{4-n}]^{2-}$ ($n = 1-4$) instead of carbonyls. The content of this ion increases during the reaction. The course of the reaction is affected by the addition of potassium acetate. With the proportions $CH_3COOK : Co^{II} = 1-2$ the reaction velocity is a maximum, and the formation of acetone is inhibited; if, however, this ratio is 4, reaction

does not take place. The formation of cobalt carbonyl is accelerated by the addition of potassium acetate [77]. Similar effects are exerted by lithium, sodium, magnesium, and manganese acetates, potassium propionate, and sodium benzoate [78]. The productivity of the catalyst is 0.1–0.2 kg litre^{-1} h^{-1}. [77] When sufficient water is present, the methyl acetate and acetone formed as byproducts are hydrolysed to methanol [79]. Another selective catalyst is nickel acetate modified with iodine [80]. The following scheme has been suggested for the reaction

$$2CoI_2 \xrightarrow[-(HI+CO_2)]{CO+H_2O} Co_2(CO)_8 \xrightarrow[-CO_2]{CO+H_2O} 2HCo(CO)_4;$$

$$CH_3OH \xrightarrow[-H_2O]{HI} CH_3I;\ HCo(CO)_4 \underset{HI}{\overset{CH_3I}{\rightleftarrows}} CH_3Co(CO)_4 \rightarrow CH_3COCo(CO)_3 .$$

Acetic acid may then be formed in two ways:

$$\underset{CO\downarrow\uparrow -CO}{CH_3COCo(CO)_3} \xrightarrow{+H_2O} CH_3COOH + \underset{CO\downarrow\uparrow -CO}{HCo(CO)_3},$$

$$CH_3COCo(CO)_4 \xrightarrow{+H_2O} CH_3COOH + HCo(CO)_4 .$$

In 1964 an installation producing 1000 metric tons of acetic acid per month was started up in West Germany [79]. Several large works are operating this process in the U.S.A. and West Germany [81–83]. Acetic acid is obtained in 90% yield based on methanol and 70% based on carbon monoxide with the use of cobalt(II) iodide at 250–260°C and 650–700 atm. In the presence of cobalt diacetate and sodium, potassium, lithium, and calcium iodides with a catalyst concentration of 1–20 mole % at 180–220°C and 300–500 atm the reaction of methanol with a mixture of carbon monoxide and hydrogen (1.5 : 1) is used to obtain acetic esters (40–60%), acetaldehyde, and the hydrogenation product of the latter—ethanol [84].

Rhodium and iridium catalysts are employed for the carbonylation of methanol under homogeneous reaction conditions—e.g. $RhCl_3.3H_2O$, $Rh_2O_3.5H_2O$, $RhCl(CO).(P(C_6H_5)_3)_2$, $(RhCl(CO)_2)_2$, $IrCl_3.3H_2O$, $Ir_4(CO)_2$, $IrCl(CO)(P(C_6H_5)_3)_2$—modified with halides and halogens (iodine, hydrogen iodide, calcium iodide dissolved in benzene, water, methanol, nitrobenzene, acetic acid) [85]. These catalysts are active at 175–250°C and low pressures, even subatmospheric, when the selectivity reaches 99%.

In the presence of a rhodium sesquioxide–carbon catalyst modified with methyl iodide or hydrogen iodide, under conditions of heterogeneous catalysis at 1–15 atm, the conversion of methanol into acetic acid and methyl acetate is 93%. [86]

The carbonylation of alcohols in the presence of α-oxides and carbonyls of cobalt, rhodium, and iridium at ~300 atm and 120–250°C has been used to prepare [87] hydroxy-carboxylic esters in yields up to 97%.

2. Reactions in the presence of Acid and Basic Catalysts

The early results on the carbonylation of alcohols in the presence of catalysts of acidic and basic character have been discussed in a previous review [71].

The carbonylation of saturated alcohols at carbon monoxide pressures of 50–90 atm and 15–70°C occurs in two stages in the presence of 96–98% sulphuric acid [88]. The first stage involves interaction of the initial alcohol, carbon monoxide, and sulphuric acid, with the assumed formation of acylsulphuric acids in equilibrium with acylium and hydrogen sulphate ions. In the second stage water or alcohol is added to the reaction mixture, which results in the formation of carboxylic acids or their esters mixed with small quantities of the free acids:

$$ROH + H_2SO_4 \xrightarrow{-H_2O} R^+ + \bar{O}SO_2OH \xrightarrow{CO} R'\overset{+}{C}O + \bar{O}SO_2OH \rightleftarrows$$

$$\rightleftarrows R'\underset{\underset{O}{\|}}{C}OSO_2OH \xrightarrow[-H_2SO_4]{HX} R'\underset{\underset{O}{\|}}{C}-X$$

where R′ is a radical isomeric with R but more branched, and X = OH, OR″. With C_{3-5} aliphatic alcohols the yield of acids and esters increases with the molecular weight of the alcohol and on passing from a straight-chain alcohol to a branched-chain isomer. The main reaction products are carboxylic acids (or their esters) containing one more carbon atom than in the initial alcohol, with a quaternary or more rarely a tertiary carbon atom in the α-position. Propyl and isopropyl alcohols give isobutyric acid, n-butanol yields α-methylbutyric acid, isobutanol forms αα-dimethylpropionic acid, n-pentanol yields a mixture of αα-dimethyl- and α-ethyl-butyric acids (1.7 : 1), and isopentanol gives αα-dimethylbutyric acid. The total yield of acids and esters from C_{6-10} alcohols is 70–95%, and varies little with the molecular weight of the alcohol [89]. Cyclohexanol yields 1-methylcyclopentanecarboxylic and cyclohexanecarboxylic acids (2 : 1), cyclopentanol gives cyclopentanecarboxylic and *cis*-decahydronaphthalene-9-carboxylic acids (20 : 1), and *p*-menthol forms methane-*p*-carboxylic acid [90]. Raising the carbon monoxide pressure from 5 yo 75 atm increases the total yield of esters on methoxycarbonylation. In the case of isobutyl alcohol the content of the αα-dimethylpropionic ester is independent of the carbon monoxide pressure at ~80%; [91] but in the case of n-pentanol the content of the α-ethylbutyric ester increases at the expense of the αα-dimethylbutyric ester, the total yield of esters at 70 atm being 82–86%. [92] The composition of the products of the methoxycarbonylation of n-pentanol is almost independent of the molar ratio of sulphuric acid to alcohol in the range 4–10. The optimum temperature in the first stage of the reaction is ~60°C. [93]

Carboxylic acids are synthesised from alcohols with formic acid as carbonylating reagent in the presence of sulphuric acid at atmospheric pressure and room temperature. Alcohols of the neopentyl type, which cannot be directly dehydrated to alkenes, also undergo the above reaction [94]. This shows that alcohols may not be dehydrated to alkenes under the influence of an acid catalyst, but may form carbonium ions directly, which then react with carbon monoxide.

Neopentyl alcohol gives αα-dimethylbutyric acid, 2,2-dimethylbutanol yields a mixture of αα-dimethylvaleric and α-ethyl-α-methylbutyric acids (1 : 2), and 1′-methylcyclopentylmethanol forms 1-methylcyclohexanecarboxylic acid. In the case of 1′-methylcyclohexylmethanol and its homologues the hydroxymethyl carbon enters an alkyl side-chain. Bicyclo[3,3,0]oct-1′-ylmethanol gives bicyclo[3,3,1]nonane-1-carboxylic acid, hexahydroindan-8′-ylmethanol yields a mixture of *cis*- and *trans*-decahydro-9-naphthoic acids, decahydronaphth-9′-ylmethanol a mixture of decahydro-1- and -2-methylnaphthoic acids contaminated with bicyclo[5,4,0]undecane-1-carboxylic acid [95,96], and adamantan-1-ol is converted into adamantanecarboxylic acid [97].

Diprimary diols give on carbonylation mainly unsaturated monocarboxylic acids and lactones contaminated with dicarboxylic acids. Nonane-1,9-diol and decane-1,10-diol yield respectively αα′α′-tetramethylpimelic acid (33%) and αα′α′-tetramethylsuberic acid (7%). [55]

The course of carbonylation of ditertiary diols of general formula $HO.CR_2.[CH_2]n.CR_2.OH$ ($n = 4-8$; $R = CH_3$, C_2H_5, $n\text{-}C_4H_9$) is not affected by increase in the size of the alkyl groups provided that the distance between the hydroxyls is maintained. 2,7-Dimethyloctane-2,7-diol ($n = 4$) forms a mixture of four isomeric C_{11} cyclic monocarboxylic acids in ~70% yield. 3,8-Diethyldecane-3,8-diol and 5,10-di-n-butyltetradecane-5,10-diol ($n = 4$) give only cyclic monocarboxylic acids (~70%), and 2,8-dimethylnonane-2,8-diol ($n = 5$) yields a mixture of monocarboxylic (40%) and dicarboxylic (42%) acids. The products from 2,9-dimethyldecane-2,9-diol ($n = 6$) and 2,10-dimethylundecane-2,10-diol ($n = 7$) are dicarboxylic acids (61–63%); the total yield of mixtures of carboxylic acids is 87%, consisting mainly of $\alpha\alpha\alpha'\alpha'$-tetramethylsebacic and $\alpha\alpha\alpha'\alpha'$-tetramethylbrassylic acids respectively, together with 16 to 24% of cyclic monocarboxylic acids. 2,11-Dimethyldodecane-2,11-diol ($n = 8$) yields a mixture of carboxylic acids (69%) containing 34% of dicarboxylic acids, mainly 2,2,11,11-tetramethyldodecanedioic acid, and monocarboxylic acids (15%) together with polymeric acids (20%), a neutral oil (15%), and polymers (10%).[55]

Carboxylic esters are obtained in two stages from alcohols and formic acid in the presence of a large excess of sulphuric acid at atmospheric pressure; in the second stage water is replaced by alcohol. This method has been used to prepare methyl $\alpha\alpha$-dimethyl- and α-ethyl-alkanoates from C_4-C_7 saturated alcohols and cyclohexanol using methanol in the second stage. The free acids are formed together with the esters. The total yield of esters and acids increases with the molecular weight of the initial alcohol and the degree of branching of its molecule[98]. 1-Methyl-, 1-ethyl-, and 1-propyl-cyclohexanols are methoxycarbonylated to form the corresponding methyl 1-alkylcyclohexanecarboxylates in yields up to 40%, cyclohexylmethanol to form methyl 1-methylcyclohexanecarboxylate, cyclopentanol to give methyl cyclopentanecarboxylate (45%) and *cis*-decahydro-9-naphthoate (2%), and 1-methyl- and 1-ethyl-cyclopentanols to yield methyl 1-methylcyclopentanecarboxylate (1%) and 1-methylcyclohexanecarboxylate (4%) respectively[99].

Concentrated orthophosphoric acid is also used as catalyst for the carbonylation of saturated alcohols by carbon monoxide. The optimum temperature for the reaction lies between 125° and 175°C, i.e. 100 deg higher than in the presence of sulphuric acid. The optimum pressure of carbon monoxide is 70–80 atm. Variation in the molar ratio of orthophosphoric acid to alcohol in the range 10–2.5 : 1 has no significant effect on the course of the reaction. The acid can be used repeatedly[100]. The main products of the carbonylation of saturated C_4-C_7 alcohols are their $\alpha\alpha$-dimethyl-, α-ethyl-α-methyl-, and α-ethyl-alkanoates together with the alkanoic acids themselves—derivatives of monomeric, dimeric, and trimeric forms of the initial alcohol—as well as products of the disproportionation of carbonium ions formed from the initial alcohol. Cyclopentanol and cyclohexanol yield only the corresponding free acids, predominantly derivatives of the dimeric form: cyclopentanol gives a mixture of *cis*- and *trans*-decahydro-9-naphthoic acids; cyclohexanol produces not only derivatives of the dimeric form but also small quantities of 1-methylcyclopentanecarboxylic and cyclohexanecarboxylic acids[101-103].

Hydrates of boron trifluoride are active catalysts for the carbonylation of alcohols. In the presence of the dihydrate at 100°C and a carbon monoxide pressure of 100 atm 2-methylpropan-1-ol gives up to 76% yields of $\alpha\alpha$-dimethylpropionic acid or up to ~90% of its isobutyl ester[104]. In the presence of the monohydrate pentan-1-ol and 3-methylbutan-1-ol form a mixture of carboxylic acids containing mainly $\alpha\alpha$-dimethylbutyric acid; the former alcohol produces also α-methylvaleric and α-ethylbutyric acids. In the presence of other hydrates of boron trifluoride, containing 1.5–3.0 H_2O, pentyl $\alpha\alpha$-dimethylbutyrate is obtained from pentan-1-ol, and the isopentyl ester from 3-methylbutan-1-ol; the yield of these esters passes through a maximum at the dihydrate as the water content is decreased[105]. Hexan-1-ol gives hexyl $\alpha\alpha$-dimethylvalerate and α-ethyl-α-methylbutyrate with maximum yields of 76% and 30% respectively, the reaction occurring only in the presence of the sesquihydrate[106]. Heptan-1-ol forms heptyl α-ethyl-α-methylvalerate and 2,2-dimethylhexanoate with respective maximum yields of 46% and 42%; if the hydrate contains more than 1.5 H_2O, hardly any reaction occurs with heptan-1-ol[106]. With pentanol and 3-methylbutanol in the presence of boron trifluoride monohydrate the reaction mixture separates into two layers—carboxylic acids and catalysts—at the end of the reaction only after water has been added. With a catalyst having a higher water content the reaction is accompanied by a sharp separation of reaction products from the catalyst phase without the addition of water, probably because of the presence of a sufficient quantity of water in the catalyst itself[107]. The reaction is represented by the scheme

$$RCH_2CH_2OH + [BF_3 \cdot (n-1)H_2O \cdot OH]^-H^+ \rightarrow R\overset{+}{C}HCH_3 + BF_3 \cdot nH_2O,$$

$$R\overset{+}{C}HCH_3 \xrightarrow{CO} R'\overset{+}{C}O \xrightarrow[-H^+]{ROH} R'COOR.$$

Mixtures of oxiran, methyloxiran, or phenyloxiran with salts (sodium, potassium, or calcium formate, acetate, or benzoate), amines, arsines, or phosphines may serve as catalysts for the carbonylation of methanol with carbon monoxide at 200 atm and 170°C. Methyl formate is obtained in yields up to 64% when the ratio by weight of salt to alkene oxide is 1 : 10. The catalytic activity is ascribed to an alkoxide ion formed, e.g. when the catalyst system comprises oxiran and triphenylphosphine, by the scheme

$$RCOO^- + \underset{\diagdown O \diagup}{CH_2—CH_2} \rightarrow RCOOCH_2CH_2O^- \xrightarrow{CH_3OH} RCOOCH_2CHO_2H + CH_3O^-,$$

$$(C_6H_5)_3P + \underset{\diagdown O \diagup}{CH_2—CH_2} \rightarrow (C_6H_5)_3P\overset{+}{C}H_2CH_2O^- \xrightarrow{CH_3OH} (C_6H_5)_3P\overset{+}{C}H_2CH_2OH + CH_3O^-.$$

The true catalyst of the latter reaction is regarded[108] as the compound

$$(C_6H_5)_3\overset{+}{P}CH_2CH_2OCH_2\overline{O}CH_3$$
(XLIII)

formed from the alcohol, oxiran, and the base.

IV. CARBONYLATION OF HALOGENO-DERIVATIVES

1. Acetylenic Halogeno-derivatives

In the presence of tetracarbonylnickel α-iodoacetylenes are reduced to acetylenic hydrocarbons, which are not carbonylated[4,57,109]. α-Chloroacetylenes form allenic acids mixed with substituted malonic acids and ketones. The carbonylation of β- and γ-halogenated acetylenes occurs more easily the more remote is the halogen from the triple bond[110-112]. Prop-2-ynyl chloride, carbon monoxide, and water in the presence of tetracarbonylnickel give a 70% yield of a mixture of butadienoic and itaconic acids[112]:

$$CH_2{=}C(COOH)CH_2COOH \xleftarrow[-HCl]{2CO+2H_2O} CH{\equiv}CCH_2Cl \xrightarrow[-HCl]{CO+H_2O} H_2C{=}C{=}CHCOOH.$$

In the presence of small quantities of water itaconic acid is the main product [111]. Prop-2-ynyl bromide reacts with tetracarbonylnickel in alcoholic solution at atmospheric pressure and 70°C to form ethyl 3-bromobut-3-enoate in ~20% yield. Reaction is less vigorous under carbon monoxide pressure, probably because in the first stage the complex of the acetylenic compound with the carbonyl is formed with the evolution of carbon monoxide [113]. It is preferable to prepare allenic acids in an aqueous–alcoholic buffer by the reaction

$$R^1C{\equiv}CCR^2R^3Cl \xrightarrow[-HCl]{Ni(CO)_4,\ H_2O} HOOCCR^1{=}C{=}CR^2R^3$$

than by means of Grignard reagents and carbon dioxide. The possibility of initial rearrangement of the α-chloroacetylene into a chloroallene is eliminated, since chloroallene does not react under these conditions [114].

In the presence of palladium dichloride at ~20°C and 100 atm carbon monoxide pressure prop-2-ynyl chloride in methanolic solution reacts with carbon monoxide to form methyl itaconate in 66% yield together with small quantities of methyl 3-chlorobut-3-enoate [61].

2. Ethylenic Halogeno-derivatives

Unsaturated acids or their esters are obtained by the carbonylation of alkenyl halides in aqueous or alcoholic solution in the presence of tetracarbonylnickel under carbon monoxide pressure. With unbranched 1-halogenoalkenes the reaction is

$$RCH{=}CHCH_2Cl + CO + R^1OH \xrightarrow{Ni(CO)_4} RCH{=}CHCH_2COOR^1 + HCl$$

accompanied by the side-reaction

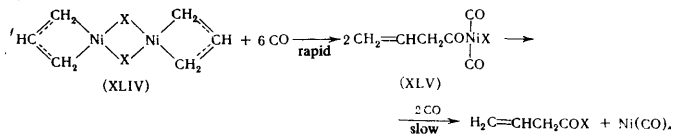
$$2\,RCH{=}CHCH_2Cl + Ni(CO)_4 \rightarrow (RCH{=}CHCH_2)_2 + 4CO + NiCl_2\ .$$

Allyl chloride yields crotonic acid by isomerisation of the initially formed but-3-enoic acid [112], but-2-enyl chloride gives pent-3-enoic acid, and 5-chloropent-3-enonitrile forms the mononitrile of dihydromuconic acid, which on hydrogenation is converted into caprolactam.

The catalytic activity of tetracarbonylnickel is explained by the intermediate formation of a complex carbonyl-π-allylnickel chloride $[Ni(CO)_3CH_2CH{:}CHR]^+Cl^-$, which breaks down under the influence of carbon monoxide and alcohol [112,114–118]. Five-coordinated nickel complexes of the type $[NiHalCO\pi\text{-allyl}.(C_6H_5)_3P]$ are assumed to be formed as intermediates in the carbonylation of allyl compounds. These complexes are obtained by the reaction of allyl halides with tricarbonyltriphenylphosphinenickel in a mixture of methanol and benzene [119]. The carbonylation of bis-π-allylnickel halide complexes (Hal = Br or I) in the presence of tetracarbonylnickel yields methyl methacrylate (50–70%) contaminated with methyl crotonate [120,121]. The main product of the carbonylation of allyl halides with carbon monoxide at 50 atm and 100°C is methyl but-3-enoate, which is also obtained by the carbonylation of bis-π-allylnickel bromide [122]. The reaction is represented by the scheme [123]

$$RCH{=}CHCH_2Br + 2\,Ni(CO)_4 \rightarrow [RCH{=}CHCH_2\cdot Ni(CO)_3]^+Br^- \rightarrow$$
$$\rightarrow RCH{=}CHCH_2COOR^1 + Ni(CO)_4 + HCl\ .$$

The carbonylation of allyl halides is conducted under milder conditions. In the reaction of π-allylnickel iodide with carbon monoxide in ether at 0°C, infrared spectroscopy has detected nickel carbonyl and butenoyl iodide. An unstable intermediate dimeric halogeno-π-allylnickel complex (XLIV) has been isolated, which can exist in ethereal solution at 0°C, and reacts rapidly with carbon monoxide to form a carbonylbutenoylnickel halide (XLV):[124]



(XLIV) (XLV)

$$\xrightarrow[slow]{2\,CO} H_2C{=}CHCH_2COX + Ni(CO)_4$$

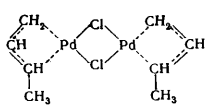
Compounds of noble metals are active catalysts for the carbonylation of unsaturated halogeno-derivatives by carbon monoxide. In the presence of palladium dichloride dehalogenation occurs at the same time, and rise in temperature favours the formation of derivatives of unsaturated acids. Vinyl chloride in benzene solution yields $\beta\beta$-dichloropropionyl chloride, but in alcoholic solution saturated with hydrogen chloride at 130°C and 600 atm the ethyl ester is obtained, and at 80°C and 100 atm a mixture of ethyl β-chloropropionate and propionate. Allyl chloride in benzene solution at room temperature and 100 atm forms 3,4-dichlorobutyryl chloride, and at 130°C but-3-enoyl chloride; in alcoholic solution at 120–170°C the products are ethyl but-3-enoate together with the but-2-enoic and isobutyric esters, and at 80°C and 100 atm a mixture of ethyl butyrate, isobutyrate, and β-chloro-α-methylpropionate. These reactions are catalysed also by metallic palladium alone and on carbon, alumina, or a zeolite.

Heating the complex of palladium dichloride with allyl chloride yields but-3-enoyl chloride [9,42,67,125–127]. This complex catalyses the carbonylation by carbon monoxide of allyl chlorides to form chlorides or esters of alk-3-enoic acids [11]. In the presence of bistriphenylphosphinepalladium dichloride the carbonylation of allyl chlorides also takes place with maintenance of the double bond:

$$CH_2{=}CHCH_2X + CO + ROH \rightarrow CH_2{=}CHCH_2COOR + HX$$

where X = Hal and R = Alk or Ar. [66] Pyridine, benzonitrile, and other compounds may also serve as ligands in palladium dichloride.

1-Chlorobut-2-ene and 3-chlorobut-1-ene react with carbon monoxide in the presence of di-π-allylchloropalladium at 100°C and 150–180 atm via the intermediate complex



(XLVI)

to form pent-3-enoyl chloride in 80% yield. 3-Methylbut-3- and -2-enoyl chlorides are obtained from 3-chloro-2-methylpropene [11]. The carbonylation of allyl chlorides in the presence of metallic palladium and rhodium, their complexes or salts, to give acid halides is accelerated by additions of acetylene, cycloheptadiene and cyclopentadiene hydrocarbons, indene, and fluorene [128].

3. Allyl Halides in the presence of Acetylene

Acetylene may enter into the reaction of allyl halides with carbon monoxide, water, or alcohol in the presence of metal carbonyls and their salts, generally tetracarbonylnickel, in hydroxylated solvents at 20–60°C to form unbranched dienoic acids or their esters. When 20% of the stoichiometric quantity of nickel carbonyl is used, $\alpha\beta : \delta\epsilon$-dienoic acids and their esters are obtained:

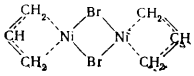
$$RCH{=}CHCH_2X + CO + R^1OH + CH{\equiv}CH \rightarrow RCH{=}CHCH_2CH{=}CHCOOR^1 + HX$$

(X = Hal). The reaction goes best at room temperature and atmospheric pressure, with yields up to 80%.[116,129,130] Allyl chloride is converted into hexa-2,5-dienoic acid and its methyl, ethyl, and other esters, which possess a pleasant odour and are stable compounds. Hepta-2,5-dienoic and 5-methylhexa-2,5-dienoic acids are obtained from but-2-enyl and methylallyl chlorides respectively. Secondary react more slowly than primary chloro-derivatives to form the same unbranched dienoic acids. Carbonylation is slowed down or completely inhibited by an electronegative substituent at the double bond. The reactions are favoured by an allyl and also by a phenyl group conjugated with the double bond[131-136]. The following mechanism has been suggested for the reaction involving tetracarbonylnickel[123]:

$$RR^1C{=}CR^2CHR^3Cl + Ni(CO)_4 \rightarrow [(CO)_3NiCHR^3CR^2{=}CRR^1]^+Cl^- \xrightarrow{C_5H_5} \rightarrow \text{cis-}[(CO)_3NiClCOCH{=}CHCHR^3CR^2{=}CRR^1 \xrightarrow{CO} \rightarrow \text{cis-}[(CO)_3NiCOCH{=}CHCHR^3CR^2{=}CRR^1]^+Cl^- \xrightarrow{CO+R^4OH} \rightarrow \text{cis-}\ RR^1C{=}CR^2CHR^3CH{=}CHCOOR^4 + Ni(CO)_4 + HCl\ .$$

The *cis*-configuration of the alkenoyl complex, which favours cyclisation, is confirmed also by the formation of up to 97% yields of acetic esters of phenols when the resulting dienoic acids are treated with acetic anhydride in the presence of zinc, aluminium, or tin(IV) chloride or sulphuric acid as catalyst[123,137].

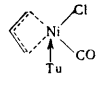
A mixture of carbon monoxide and acetylene reacts with the dimer of π-allylnickel bromide (XLVII) in ether at 0°C to form a dienoyl bromide[124]:



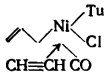
(XLVII)

$$+ 10\,CO + 2\,C_2H_2 \rightarrow 2\,CH_2{=}CHCH_2CH{=}CHCOBr + 2\,Ni(CO)_4\ .$$

The carbonylation of allyl compounds by carbon monoxide in the presence of acetylene can be accomplished in three ways—by the use of nickel carbonyl previously prepared at 20°C and atmospheric pressure, by generating an intermediate compound as catalyst *in situ* at the same temperature and pressure, and finally by using nickel compounds at 150–200°C and pressures of carbon monoxide and acetylene of 30–100 atm—the latter two of which did not require use of the extremely toxic tetracarbonylnickel. For example, a mixture of Raney nickel with thiourea or a mixture of nickel dichloride, thiourea, and iron powder is employed, when the nickel chloride is reduced by the iron powder[117,131,138]. The catalyst may be the five-coordinated nickel complex formed by reducing nickel dichloride hexahydrate with an iron alloy containing 80% of manganese and with thiourea as ligand[139]. The structure of the complex was based on data on five-coordinated halogeno(carbonyl)triphenylphosphine-π-allylnickel[140] and halogeno(thiourea)-π-allylnickel[141] complexes. In the presence of carbon monoxide and acetylene at room temperature and atmospheric pressure the complex catalyst converts methanolic allyl chloride into methyl hexa-2,5-dienoate in ~75% yield. The chief side-products are hexa-1,5-diene, methyl but-3-enoate, 2-oxocyclopent-3-enylacetate, and γ-oxo-δ-2-oxocyclopent-3-enylvalerate, phenyl hexa-2,5-dienoate, and *S*-allylisothiourethane chloride. The five-coordinated nickel complex

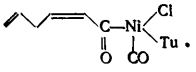


(Tu = thiourea) gives hexa-1,5-diene with allyl chloride, methyl but-3-enoate with carbon monoxide, and *S*-allylisothiourethane chloride with urea[139]. These molecules easily displace acetylene from the complex



(XLVIII)

before reaction with the allyl group. In the presence of carbon monoxide this reaction yields



(XLIX)

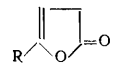
This is followed either by cyclisation to a cyclopentene ring and then the formation of methyl 2-oxocyclopent-3-enyl acetate on the absorption of carbon monoxide, or by cyclisation to phenol and its reaction with carbon monoxide to form phenyl hexa-2,5-dienoate. Further reactions of the 2-oxocyclopent-3-enylacetic ester followed by hydrogenation of the double bond lead to formation of the γ-oxo-δ-2-oxocyclopent-3-enylvaleric ester[142,143].

The course of the reaction is affected by the nature of the solvent. When allyl halides react with carbon monoxide and acetylene in the presence of tetracarbonylnickel in ethereal or ketonic solution, the main products are not unsaturated acids and their esters, as is observed in aqueous or alcoholic medium, but cyclopentenonic acids or lactones. In a ketone solution allyl halides with electron-accepting substituents give satisfactory yields of the corresponding dienoic acids[144]. Acetone, ethyl acetate, dioxan, and oxolan are used as solvents. Methylallyl chloride yields derivatives of cyclohexane and bicyclo-[3,1,0]hexane; but allyl bromide yields hexa-2,5-dienoic and 2-oxocyclopent-3-enylacetic acids, and also lactones of 4-hydroxy-2-isopropylidene-5-(2-oxocyclopent-3-enyl)-pent-3-enoic and 4-hydroxy-5-(2-oxocyclopent-3-enyl)-pent-3-enoic acids. The reaction of allyl chloride with propyne in the presence of tetracarbonylnickel in aqueous acetone leads to the formation of 4-methyl-5-oxocyclohex-3-enecarboxylic acid[145].

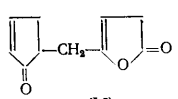
The reactions of allyl halides in ketone solutions are accompanied by the intermediate formation of carbonylhexadienoylnickel chloride[146]. The effect of the solvent on the reaction is due to stabilisation of the acyl group resulting from donor–acceptor interaction with the carbonyl group of the solvent, perhaps in a complex of the type

$$[R^1R^2C\dot{O}{-}CRO{-}\dot{N}i(X)CO].$$

Allyl chloride, carbon monoxide, and substituted acetylenes in the presence of tetracarbonylnickel yield ketone and lactone derivatives containing oxocyclopentenylacetic and oxocyclohexenecarboxylic acids. An intermediate complex of the acetylenic compound with the carbonyl reacts with allyl chloride to close the cyclopentene or cyclohexene ring with the addition of carbon monoxide. After this the ring opens to form the acid or, with further addition of carbon monoxide and acetylene, also ketones and lactones[147]. In ketone solutions allyl halides, acetylene, and carbon monoxide in the presence of tetracarbonylnickel form $\beta\gamma$-unsaturated γ-lactones of the types[146,148,149]

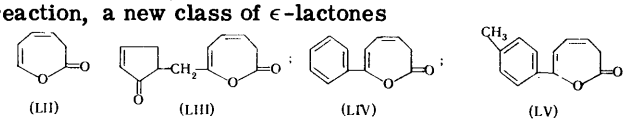


(L)



(LI)

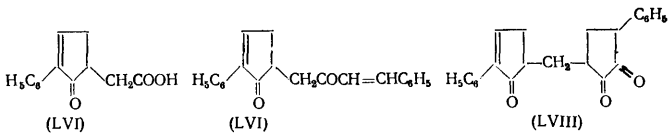
The reaction takes place with the stoichiometric quantity of the carbonyl at 40–50°C. If the concentration of carbon monoxide is low, and water is added at the end of the reaction, a new class of ϵ-lactones



(LII) (LIII) (LIV) (LV)

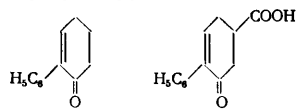
is obtained having two double bonds in the ring. They are formed by the addition of two molecules of acetylene and one molecule of carbon monoxide to an acyl group followed by lactonisation [150].

In the reaction of allyl halides with phenylacetylene and tetracarbonylnickel the allyl group usually adds by means of its primary carbon atom to the unsubstituted carbon in the acetylene, whereas the carbonyl group attacks the hydrocarbon on the opposite side, to form the compound $CH_2:CHCH_2CH:C(C_6H_5)CONiX$. Ring closure results in the formation of cyclopentenone derivatives



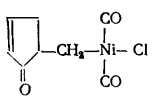
(LVI) (LVI) (LVIII)

or cyclohexenone derivatives

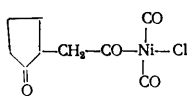


(LIX) (LX)

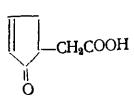
together with γ-lactones similar to the above [151]. The carbonylation of allyl halides with cyclisation is stereospecific. *cis*-Hexa-2,5-dienyl chloride reacts with tetracarbonylnickel in diethyl ether, benzene, or heptane forming



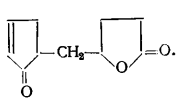
or



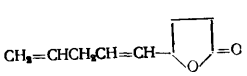
in both of which the carbonyl group can be replaced by other ligands, but in the absence of acetylene



is formed. In the presence of acetylene the course of the reaction is strongly dependent on the solvent; in a ketone medium a γ-lactone



is formed. *trans*-Hexa-2,5-dienyl chloride is not cyclised under the same conditions, but reacts similarly to an acid chloride. In acetone it is mainly converted into a γ-lactone [152].



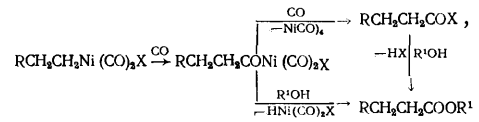
4. Saturated Halogeno-derivatives

(*a*) Catalysts based on Group VIII metals

The preparation of carboxylic acids from alkyl halides, carbon monoxide, and water is accomplished in the presence of tetracarbonylnickel at 350–450°C and 100 atm.[153,154] The alkyl halide may react directly with the carbonyl [124]:

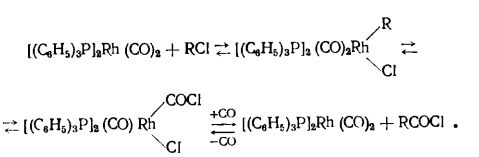
$$Ni(CO)_4 + RCH_2CH_2Cl \rightarrow RCH_2CH_2Ni(CO)_3X,$$

Reaction then takes place with carbon monoxide and an alcohol:



Cobalt carbonyls also catalyse this reaction. In the presence of sodium tetracarbonylcobaltate in alcoholic solution at atmospheric pressure carboxylic esters are obtained in yields up to 80% from alkyl halides. Methyl iodide gives an acetic ester, pentyl iodide forms a hexanoic ester, and 1-chloro- and 2-iodo-octanes give a nonanoic ester. Other catalysts are pent-4-enoyltricarbonylacrylonitrilecobalt, tricarbonyl-π-allylcobalt, acetyltricarbonyltriphenylphosphinecobalt, and sodium tetracarbonylferrate [155]. Ethyl butyrate and isobutyrate are obtained from butyl iodide and carbon monoxide in the presence of potassium tetracarbonylcobaltate in an alcoholic medium. Isomeric compounds are formed by the isomerisation of alkyl- and acyl-cobalt tricarbonyls [156]. In the presence of bistetracarbonylcobalt aldehydes are obtained from alkyl halides and mixtures of carbon monoxide and hydrogen in the proportions 1:4–4:1 at 130–140 atm and 160°C: e.g. octyl bromide yields nonanal (90%). [157] Fluoroalkenes form a complex with bistetracarbonylcobalt at 100°C: tetrafluoroethylene yields μ-tetrafluoroethylene-bistetracarbonylcobalt $(CO)_4Co.CF_2:CF_2.Co(CO)_4$. [158]

Rhodium(II) complexes are also effective catalysts for the carbonylation of alkyl halides to form halides of carboxylic acids [159]. The reaction with chloro-carbonyl-bistriphenylphosphinerhodium(II) can be written [160]



(*b*) Acid catalysts

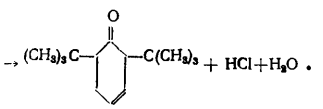
High yields of acid chlorides are obtained by the reaction of alkyl chlorides with carbon monoxide (at 120 atm) in the presence of aluminium trichloride at 50°C. Polyhalogenated alkanes react at 200°C and 900 atm. Carbon tetrachloride gives a 37% yield of trichloroacetyl chloride, chloroform 21% of dichloroacetyl chloride, and dichloromethane 2% of chloroacetyl chloride. Compounds $C_6H_{6-n}Cl_{n-1}COCl$ and $C_2H_{6-n}Cl_n$ are formed in low yields. [161] In the presence of iron trichloride the reaction takes place under milder conditions (150°C and 50 atm), but with still smaller yields [162]. The following

series of reactions is assumed between t-butyl chloride and carbon monoxide (150 atm) in the presence of aluminium or iron(III) chloride at 5°C:[163]

$$(CH_3)_2C{=}CH_2 + HCl \rightleftarrows (CH_3)_3CCl \overset{+CO}{\underset{-CO}{\rightleftarrows}}$$

$$\rightleftarrows \underset{6-12\%}{(CH_3)_3CCOCl} \overset{+CH_2=C(CH_3)_2}{\rightleftarrows} \underset{12-21\%}{(CH_3)_3CCOCH{=}C(CH_3)_2} + HCl;$$

$$(CH_3)_2C{=}CH_2 + 2\,(CH_3)_3CCOCl \xrightarrow[-AlCl_4^- \text{ or } FeCl_4^-]{AlCl_3 \text{ or } FeCl_3}$$



$$\rightarrow (CH_3)_3C\text{–}C_6H_4\text{–}C(CH_3)_3 + HCl + H_2O\,.$$

Carboxylic acids are prepared from alkyl halides, carbon monoxide, and water in the presence of hydrogen fluoride at 150°C and 45 atm[164]. With carbon monoxide and hydrogen fluoride in the presence of boron trifluoride secondary alkyl chlorides and bromides give high yields of the fluorides of carboxylic acids[165]. t-Pentyl chloride reacts with carbon monoxide and water at high pressures of the former in the presence of silver perchlorate or fluoroborate in nitrobenzene solution to form $\alpha\alpha$-dimethylbutyric acid in quantitative yield[166]. Alkyl halides are converted into carboxylic acid by using, instead of carbon monoxide, formic acid with a large excess of concentrated sulphuric acid at atmospheric pressure and 20–40°C. This method has been employed to obtain α-methylbutyric acid (30%) from s-butyl chloride, and $\alpha\alpha$-dimethylpropionic acid (76%) from t-butyl chloride[167,168]. In the presence of boron trifluoride dihydrate at 25°C and 150 atm methylallyl chloride yields chloro-$\alpha\alpha$-dimethylpropionic acid, and in the presence of a mixture of orthophosphoric acid and boron trifluoride at 70°C and 50 atm carbon monoxide pressure 8-bromo-octene gives a mixture of two isomeric acids—7-bromo-2,2-dimethylheptanoic and 6-bromo-2-ethyl-2-methylhexanoic[169].

Ethyl fluoride in anhydrous hydrogen fluoride under carbon monoxide pressures of 40–400 atm at 120–180°C is converted into a high yield of propionic acid, the reaction being catalysed by the hydrogen fluoride[170]:

$$C_2H_5F \rightarrow C_2H_5^+ + F^-;\ C_2H_5^+ + CO \rightarrow C_2H_5CO^+ \xrightarrow{F^-} C_2H_5COF\,.$$

5. Aromatic Halogeno-derivatives

Aromatic acyl fluorides can be prepared from aryl halides in the presence of tetracarbonylnickel and sodium fluoride at 380°C and 600 atm of carbon monoxide[171]. The same compounds are formed when arenediazonium fluoroborates are heated with carbon monoxide in absolute alcohol saturated with hydrogen chloride in the presence of tetracarbonylnickel[172]. Aryl iodides and acetylene in the presence of this carbonyl at 120–140°C and 30 atm give high yields of γ-keto-acids[173]:

$$C_6H_5I + C_2H_2 + Ni(CO)_4 + ROH + HX \rightarrow C_6H_5COCH_2CH_2COOR + NiIX + 2CO$$
(X=OH, OR, Cl, Br, I; R=Alk.)

Chloro- and iodo-benzenes in the presence of nickel and its di-iodide (1 : 3) under 240–320 atm of carbon monoxide at 250–300°C give 95–100% yields of benzoic acid. This method is used to prepare terephthalic (~ 30%), *o*-toluic (60%), 2-naphthoic (52%) acids[174]. An unusual reaction takes place with aryl halides at 250 to 375°C and 300–600 atm of carbon monoxide in toluene or cyclohexane solution in the presence of tetracarbonylnickel and an alkali-metal carbonate or phosphate: bromobenzene gives a mixture of phthalic anhydride (up to 75%) and benzoic anhydride (intermediate product) with benzene, *p*-chlorotoluene forms 4-methylphthalic anhydride (20%), *o*-bromotoluene produces 3-methylphthalic anhydride (45%), *p*-bromobiphenyl yields phenylphthalic anhydride (35%), and 1-chloronaphthalene gives naphthoic anhydride (4%).[175,176] In the presence of alloy catalysts formed by nickel with copper and chromium singly and together methyl terephthalate is obtained in 55–80% yield from *p*-dichlorobenzene, carbon monoxide, and methanol at 250–450°C and 200–1500 atm. Under similar conditions trichlorobenzene is converted into a mixture of benzene-mono-, -di-, and -tri-carboxylic esters[177]. Raney nickel catalyses the formation of carboxylic acids from aryl halides and carbon monoxide at 210–320°C and 100 atm[178]. Nickel formate and dichloride are less active in this reaction.

In the presence of small quantities of tetracarbonylnickel and water at 190–260°C and 200 atm aryl bromides are converted into the corresponding carboxylic acids. Additions of potassium acetate and sodium benzoate increase the yield of acids to 90% and above by keeping down the concentration of the strongly inhibiting hydrogen bromide formed in the reaction. The rate of the reaction is directly proportional to the concentrations of bromobenzene, tetracarbonylnickel, and water and inversely proportional to the pressure of carbon monoxide. When the composition of the reaction mixture is close to stoichiometric, the yield of aromatic carboxylic acids in the presence of nickel diacetate tetrahydrate at 250–260°C increases sharply[179].

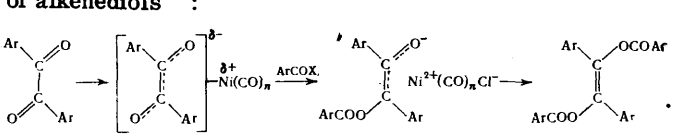
Methyl *p*-chlorobenzoate and dimethyl terephthalate are obtained in 30% and 10% yield respectively from *p*-dichlorobenzene in the presence of dicarbonylbistriphenylphosphinenickel in methyl acetate under 350 atm of carbon monoxide at 345–360°C.[180] In benzene solution under 250–350 atm of carbon monoxide at 200–300°C, with the complex $((C_6H_5)_3P)_2NiBr_2.C_4H_9Br$ or a mixture of nickel and iodine as catalyst, a mixture of terephthalic (17–25%) and *p*-chlorobenzoic (75–83%) acids is obtained[181]. The carbonyls of nickel[182–184], cobalt[185,186], and iron[185] are also used in this reaction. *p*-Chlorobenzoic acid, which is an intermediate in the synthesis of terephthalic acid, may be formed either from the acid chloride obtained from carbon monoxide and dichlorobenzene[181] or via a complex of the catalyst with dichlorobenzene[182]. However, the true reaction mechanism has not been finally elucidated.

Tetracarbonylnickel is able to undergo different stoichiometric reactions with aryl halides depending on the solvent employed. Boiling an aryl iodide with the carbonyl and a solvent is assumed to produce an intermediate complex (LXI), which in alcoholic solution then gives esters in quantitative yield, but in an aprotic solvent, e.g. oxolan or n-hexane, is converted into a diketone:

$$ArI + Ni(CO)_4 \rightarrow \underset{(LXI)}{ArCONi(CO)_nI} \rightarrow \begin{cases} \xrightarrow{ROH} ArCOOR + HI + Ni(CO)_n \\ \xrightarrow{oxolan} ArCOCOAr + NiX_2 + CO \end{cases}$$

$$\rightarrow ArC{=}CAr \quad (ArCOO,\ OOCAr)$$

Aryl chlorides, aryl bromides, and alkyl halides do not react with the carbonyl under these conditions[187–190]. Sterically hindered aryl iodides, such as *o*-tolyl and 1-naphthyl iodides, form not only diketones but also esters of alkenediols[188]:



Esters are obtained by the reaction of aryl halides with carbon monoxide and alcohols under high pressures at 350–400°C in the presence of nickel, cobalt, and strontium salts, especially the chlorides, nitrates, naphthenates, and oleates [191].

The reaction of benzyl chloride with potassium tetracarbonylcobaltate has led to the isolation not only of phenylacetyltricarbonylcobalt but also of *o*-toluoyltricarbonylcobalt, an isomerisation product whose formation is strongly promoted by adding hydrogen tetracarbonylcobaltate and also by conducting the reaction in an atmosphere of nitrogen. This isomerisation, which is not observed at 0°C, already occurs at 30–50°C. [192]

Aryl and cycloalkyl halides undergo carbonylation in the presence of palladium, its salts, and its complexes [127,128,193]. This involves the intermediate formation of a complex similar to that obtained in the decarbonylation of acid halides to aryl halides at 35–60°C. [194] The carbonylation of aryl halides takes place also in the presence of alkali metals at 300–380°C and 5–500 atm of carbon monoxide to form high yields of carboxylic acids. Excess of water stops the reaction. Intermediate formation of an alkali-metal formate is assumed [195–197].

Esters are obtained in up to 95% yield from aryl halides and certain alkyl halides in methanolic or butanolic medium in the presence of tetracarbonylnickel and potassium or sodium methoxide or butoxide. The relative proportions of halide, carbonyl, and alkoxide are 1:6:1–3. The reactivity of the halides increases in the sequence RCl < RBr < RI. The system containing the t-butoxide is considerably more active than that containing the methoxide [198].

Among non-aromatic cyclic halogeno-derivatives that undergo carbonylation are also those of adamantane. 1-Bromoadamantane and carbon monoxide in the presence of an acid catalyst yield adamantanecarboxylic acid [199].

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The results cited in this Review show that catalysts based on nickel, cobalt, and rhodium carbonyls are the most active in the carbonylation of the compounds under consideration [200]. Catalysts based on platinum and palladium chlorides are also extremely active in the carbonylation of halogeno-derivatives. Carbonylation of almost all the compounds takes place also in the presence of acid catalysts such as sulphuric, orthophosphoric, and hydrofluoric acids, boron trifluoride, etc. Special interest attaches to the possibility of effecting the reaction in the presence of these catalysts at atmospheric pressure, with the use of formic acid as carbonylating agent. Carbonylation catalysts based on Group VIII metals, especially with the addition of phosphines, arsines, and amines, are usually more selective than acid catalysts.

So called "stoichiometric" methods, in which tetracarbonylnickel is most often the source of the carbonyl group, can be used as well as catalytic methods.

The conditions of carbonylation and the nature of catalysts and solvents have a marked effect on the course of the reactions. Thus unsaturated monocarboxylic and saturated dicarboxylic acids and their esters, lactones, and chlorides can be obtained from di- and poly-unsaturated hydrocarbons. Saturated and unsaturated acids, their esters, and lactones have been obtained from alcohols. Halogeno-derivatives yield saturated and unsaturated acids, their esters, $\alpha\beta:\gamma\epsilon$-dienoic acids and esters, the difficultly accessible $\beta\gamma$-unsaturated γ-lactones, chloroalkanoic and chloroalkenoic esters, and acid chlorides and fluorides of carboxylic acids.

The production of acetic acid from methanol and the carbonylation of cyclododeca-1,5,9-triene in order to obtain 13-tridecalactam have been accomplished on an industrial scale.

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Zelinskii Institute of Organic Chemistry,
USSR Academy of Sciences,
Moscow

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2-Arylindane-1,3-diones—A New Class of Radical-active Compounds

V.V.Moiseev and I.T.Poluktov

Being cyclic β-diketones, 2-arylindane-1,3-diones play an active part in radical reactions: they react vigorously with stable radicals, inhibit the autoxidation of hydrocarbons and polymers, accelerate radical polymerisation, are effective chain-transfer agents in polymerisation, and are oxidised by oxygen and inorganic oxidants. In several radical reactions they behave like phenols, and are more reactive than the latter. A list of 141 references is included.

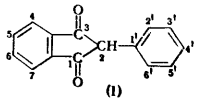
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I. INTRODUCTION

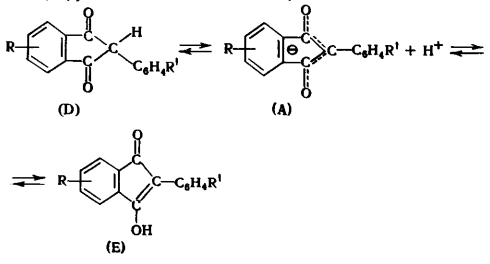
Phenols, amines, thiols, sulphides, and phosphorus-containing compounds are the main classes of organic compounds which actively influence radical reactions. They are widely used as inhibitors of the autoxidation of organic compounds in the liquid phase, stabilisers for polymers, regulators of polymerisation, and inhibitors of radical polymerisation[1-6].

During recent years a new class of radical-active compounds, 2-arylindane-1,3-diones, has been attracting the interest of research workers. The best known representative of this type is 2-phenylindane-1,3-dione



(I)

which was first synthesised in 1893 by Nathanson[7]. In the past a great deal of work was done on the preparation of its derivatives. The synthesis of 2-arylindane-1,3-diones is quite simple and can be accomplished by several methods[8-15]. All known 2-arylindane-1,3-diones are crystalline compounds, several of which are coloured[16]. They can exist in three forms[17]—in the diketo-form (D), as an anion (A), and as an enol (E):



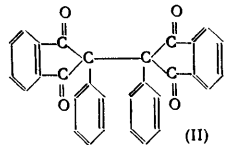
(D) (A) (E)

Equilibrium is established between these forms depending on the nature of substituents, the pH of the solution, and the medium, which makes 2-arylindane-1,3-diones extremely useful subjects for investigation from many points of view. Work on the preparation of substituted derivatives was stimulated by their practical application as blood anticoagulants. 2-Phenylindane-1,3-dione has been used in medical practice under the name "Fenilin".[10]

Although the first radical reactions were observed long ago by Nathanson, study of the oxidation of 2-phenylindane-1,3-dione by oxides of nitrogen and other oxidants was only the beginning of the investigation of these reactions as applied to 2-arylindane-1,3-diones. The need to study the behaviour of these compounds in radical reactions has arisen[18] as part of the problem of the interrelationship of structure, reactivity in homolytic reactions, and physiological activity in a series of indane-1,3-dione derivatives. Although the latter two relations could not be established[19,20], examination of the radical reactions of 2-arylindane-1,3-diones was of intrinsic practical and theoretical interest. The first systematic investigation[21] and subsequent work together with researches by other investigators have shown that these are radical-active compounds with a wide range of action. They react vigorously with stable radicals, inhibit liquid-phase oxidations, and stabilise polymers. They have a peculiar influence on radical polymerisation, acting as accelerators and regulators. In several cases 2-arylindane-1,3-diones are more effective than known compounds of other classes in their reactivity.

II. OXIDATION OF 2-ARYLINDANE-1,3-DIONES BY OXYGEN

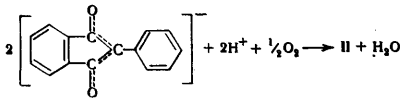
2-Arylindane-1,3-diones are quite easily oxidised by oxygen. The prolonged boiling[22] of an alcoholic solution of 5-methyl-2-phenylindane-1,3-dione in air produces dimerisation. In sodium hydrogen carbonate solution 2-phenylindane-1,3-dione is converted into the dimer—1,2-diphenyl-1,2-diphthaloylethane



(II)

in six weeks; an alcoholic solution of the diketone is decolorised in three weeks[23]. Methanolic solutions of 2-arylindane-1,3-diones are more stable than aqueous solutions[24]. Sodium 1,3-dioxo-2-phenylindane-4-sulphonate(III) is the least stable among these compounds: aqueous solutions of concentration 10^{-4} M at pH 4.3, 10^{-3} M,

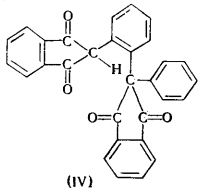
and 10^{-2} M undergo 50%, 30%, and 5% decomposition respectively in 1 h. The rate of oxidation of (III) depends on pH: the compound is most stable at pH 0, the rate of oxidation increasing with change in hydrogen-ion concentration in either direction. In strongly alkaline media, containing few hydrogen ions, a 0.001 M solution of (III) is almost unchanged after 1 h. The part played by hydrogen ions in the conversion of sodium 1,3-dioxo-2-phenylindane-4-sulphonate is indicated by the considerable rise in pH observed during the oxidation. It is suggested that the oxidation of 2-phenylindane-1,3-dione to a dimer takes place via a conjugated anion:



A kinetic study by Sztark[25] has shown that the oxidation of 2-phenylindane-1,3-dione in aqueous solution is a first-order reaction with a rate of 2.45×10^{-4} h^{-1} at 20°C and pH 12. The activation energy is 6.164×10^{-4} J $mole^{-1}$ deg^{-1}. The mean temperature coefficient of the reaction is 1.7. The extrapolated half-decomposition time at 20°C is 164 days.

Fig. 1 shows the pH dependence of the rate of oxidation of 2-phenylindane-1,3-dione. The diketone is seen to be most stable at pH 9.

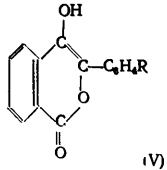
The oxidation of 2-arylindane-1,3-diones by oxygen can occur in two ways—with the formation of dimers as above and of 4-hydroxyisochroman-1-ones[26,27], which are then converted into acids and derivatives of benzoylphthalide. The dimer (II) is always formed when 2-phenylindane-1,3-dione is oxidised in alcohol, in ether, and also in pyridine in the presence of copper(I) bromide[28,29]. In this case oxidation is rapid, and together with (II) a small quantity of an isomeric dimer



(IV)

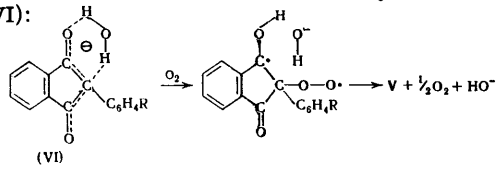
2-phenyl-*o*-phenylenebis-2,2′-indane-1,3-dione, is also isolated. The structure and the reactions of the dimer (II) have been studied quite fully[30-33]. 2-*p*-Methoxyphenylindane-1,3-dione in toluene at room temperature is easily dimerised by the action of oxygen[34]; oxidation of 2-*p*-dimethylaminophenylindane-1,3-dione has been observed during synthesis[35].

In an alkaline medium at 60–80°C 2-arylindane-1,3-diones are converted into substituted isocoumarins[27,36-39]



(V)

It has been suggested[38] that the conversion in alkaline aqueous solution involves oxidation of a hydrated diketone anion (VI):



(VI)

The addition of copper salts to an alkaline solution of 2-phenylindane-1,3-dione not only accelerates oxidation but also changes the composition of the products[27]: both 4-hydroxy-3-phenylisochroman-1-one and the dimer (II) are formed. The quantity of dimer increases with increase in the concentration of copper ions. The formation of various acids in the oxidation of 2-phenylindanedione is probably due to further oxidation and conversion of the 3-phenyl derivative (V) in alkaline medium, although this is a matter of controversy[40]. Substituted 4-hydroxy-3-phenylisochroman-1-ones are formed also when 2-arylindanediones undergo oxidation in the presence of amines[34,41]. The oxidation of diketones is accelerated by amines. Vanag and Pilegis[42] noted the formation of complexes of 2-phenylindanedione with amines.

Ozolina and Neilands[43-46] observed the oxidation by atmospheric oxygen of biphenyl and diphenyl oxide analogues of 2-arylindanediones.

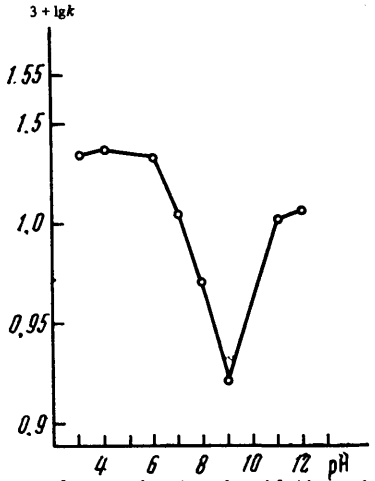


Figure 1. Dependence of rate of oxidation of 2-phenylindanedione on pH of solution.

III. ACTION OF INORGANIC OXIDANTS

In 1893 Nathanson[7] first obtained 1,2-diphenyl-1,2-diphthaloylethane (II) by passing oxides of nitrogen into an alcoholic solution of 2-phenylindane-1,3-dione. The action of pentyl nitrite produced a similar result. Boiling an alcoholic solution of 2-phenylindanedione with sodium nitrite became a simple and convenient method[7,21,23] for obtaining the dimer (II) as well as dimers[22] from substituted 2-phenylindanediones.

Formation of dimers is observed also when substituted indane-1,3-diones are treated with other oxidants. Nitric acid[47] oxidises 2-*m*-tolylindanedione; the dilute acid causes[48,49] dimerisation of the 2-*p*-nitrophenyl and 2-*p*-methoxyphenyl compounds. The nitration of 4,5-dimethoxyindane-1,3-dione produces as byproduct[50] a dimer of 4,5-dimethoxy-2-nitroindanedione. 2-Arylindanediones are easily oxidised by iodine[33,51,52] and by potassium hexacyanoferrate(III)[22,51] in an alkaline medium:

$$\Phi^- + Fe(CN)_6^{3-} \rightarrow \Phi^{\cdot} + Fe(CN)_6^{4-}$$

$$2\,\Phi^{\cdot} \rightarrow \Phi{-}\Phi$$

where Φ^- is the anion of 2-phenylindane-1,3-dione.

2-Methylindane-1,3-dione is oxidised to a dimer by potassium persulphate[53,54]. Substituted 2-phenylindanediones are oxidised to the corresponding dimers by potassium hexacyanoferrate(III), ammonium persulphate, and iron(III) chloride[55,56]. Ethyl 1,3-dioxoindanecarboxylate dimerises under the influence of lead dioxide[57]. Dimers are formed from 2-arylindanediones also in other reactions—in the thiocyanation[58] of the 2-halogeno-derivatives, in the interaction[59,60] of 2-bromo-2-*p*-nitrophenylindanedione with various amines, on treatment[61] of 2-bromo-2-phenylindanedione with alcoholic ammonia and with copper powder, and also on interaction with sodium 2-phenylindanedione. Dimers are formed also[62,63] when 2-aryl-2-iodoindanediones are heated and when 2-nitro-2-*p*-nitrophenylindanedione is boiled in anhydrous carbon tetrachloride or acetic acid[27]. Heating 2-bromo-5-methyl-2-phenylin-

anode both in alkaline[73-77] and in acid[77-82] media. Current–voltage measurements with a controlled current have been successfully applied to the anodic oxidation of β-diketones. In an alkaline medium the 2-arylindanedione anion undergoes oxidation; but in an acid medium the anodic current is maintained by oxidation of the enolic form[82]. In both cases the oxidation products are assumed to be the corresponding dimers. Table 1 lists the oxidation potentials relative to the saturated calomel electrode of the anions $E^{A}_{1/2}$ [74] and of the undissociated enolic forms $E^{E}_{1/2}$ [80] of substituted 2-phenylindanediones. These results clearly show the influence of substituents on the ease of electrochemical oxidation: electron-donating substituents considerably facilitate oxidation; the effect of substituents in the phthaloyl fragment[77] is considerably more complicated.

atom, activation energies E, and pre-exponential factors k_0 for reaction of the radical with the above compounds in dioxan at 20°C. The activation energy could not be determined for 2-naphth-2′-ylindane-1,3-dione, since it is obviously very small. The values found for the rate constants and activation energies for the 2-arylindanediones are close to those for the corresponding reaction of DPPH with phenols[99-101].

Table 2. Rate constants for the reactions of diphenylpicrylhydrazyl with 2-arylindanediones.

Aryl	a	k_1, M^{-1} min^{-1}	E, kcal $mole^{-1}$	k_0, M^{-1} min^{-1}
Phenyl	1.9	$7.9 \cdot 10^2$	5.5	$1.0 \cdot 10^7$
p-Chlorophenyl	1.7	$16.8 \cdot 10^2$	2.8	$2.0 \cdot 10^5$
p-Bromophenyl	1.7	$17.2 \cdot 10^2$	—	—
Naphth-1′-yl	1.6	$0.41 \cdot 10^2$	7.5	$1.6 \cdot 10^7$
Naphth-2′-yl	1.4	$40 \cdot 10^2$	—	—

The reason for the sharp decrease in reactivity of 2-naphth-1′-ylindanedione (XIX) is the same as in *ortho*-substituted 2-phenylindanediones (XVI and XVII). The nuclear magnetic resonance spectra show[65] that in 2-mesitylindanedione (XVI) the plane of the mesityl ring is perpendicular to that of the indanedione ring, and rotation of the former ring is retarded. The appearance of additional electronic effects in 2-arylindanediones on *ortho*-substitution is confirmed by the ultraviolet spectra[102] and by a change in acidity[17]. Thus the introduction of an *ortho*-substituent disturbs the configuration of the molecule, which leads to a change in mobility of the 2-hydrogen atom in the indanedione ring.

The difference in properties between 1- and 2-substituted naphthalene derivatives attracted attention long ago[103-105] and has been termed an "edge" effect[103], *peri*-interaction[105]. In the field of β-diketones it has been noted that iodo-derivatives[63] of 2-naphth-2′-ylindanedione are thermally less stable than the corresponding naphth-1′-yl derivatives. The construction of Stuart–Briegleb models of compounds (I), (XVI), (XVII), (XIX), and (XX) confirms that, in the *ortho*-substituted derivatives and also in (XIX), the molecular configuration is disrupted by interaction of the substituent and the carbonyl group; the aryl radical in these compounds is unable to rotate freely as in (I) and (XX).

Heating 2-phenylindane-1,3-dione with benzoyl peroxide

constants K determined for azoisobutyronitrile by means of 2-phenylindanedione, and also the initiator efficiencies β in toluene and chlorobenzene at 80°C, show complete agreement with values[109] obtained by other methods. It is interesting that unlike known inhibitors—phenols and amines—the stoichiometric coefficient of inhibition for 2-phenylindanedione is in this case unity. Thus the use of 2-arylindanediones to estimate radicals has certain advantages over such inhibitors as 1-naphthylamine and 1-naphthol in view of the simplicity of quantitative control and the definiteness of the conversion products of the inhibitor. Quantitative determination of 2-phenylindanedione and its analogues can be accomplished also spectrophotometrically[110-114], polarographically[115], bromatometrically[116], by anodic volt–amperometric measurements[76], potentiometrically[117], and by other methods[72].

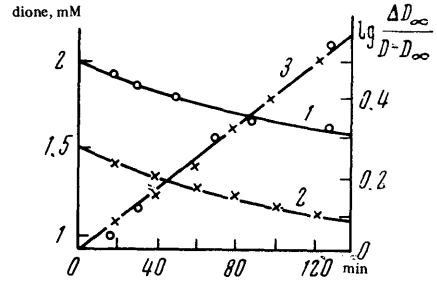


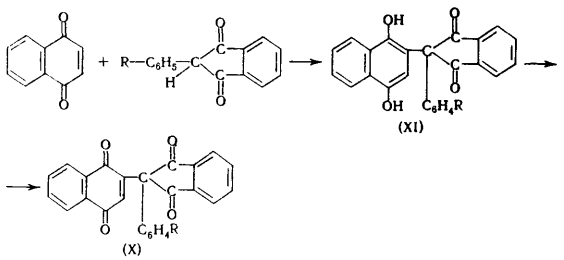
Figure 2. Consumption of 2-phenylindanedione and variation of $\lg [\Delta D\infty/(D - D\infty)]$ with time in experiments on the decomposition of azoisobutyronitrile (0.0005 M) in toluene at 80°C: 1), 2) rate curves; 3) optical density.

VI. 2-ARYLINDANE-1,3-DIONES AS OXIDATION INHIBITORS IN THE LIQUID PHASE

The reaction with radicals such as 2,2-diphenyl-1-picrylhydrazyl suggested that 2-arylindane-1,3-diones would retard the oxidation of alkylarenes by oxygen. An inhibiting effect was shown[118] in the oxidation of *p*-di-isopropylbenzene at 100°C: in the presence of 0.06 mole % of 2-phenylindanedione oxidation was delayed for 25 h.

With substituted indane-1,3-diones the reaction may also go differently: thus the interaction of 2-methylsulphonylindanedione with the quinone involves cross recombination of the 1,3-dioxoindanyl radical and of the semiquinone to form 2-(2,3-dichloro-5,6-dicyano-4-hydroxyphenoxy)-2-methylsulphonylindane-1,3-dione.

2-Arylindane-1,3-diones react with 1,4-naphthaquinone[89] in aqueous acetone solution in the presence of an acetate buffer to form a 2-(2-aryl-1,3-dioxoindan-2-yl)naphthaquinone (X), presumably[89] by the oxidation of the intermediate naphthaquinol (XI) by atmospheric oxygen:



(XI)

(X)

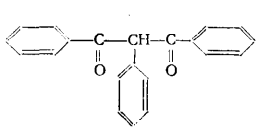
In this case dimers were not isolated. The Reviewers hold a different opinion on the course of the reaction: the first stage is 1,4-addition, the product (XI) is oxidised by the initial 1,4-naphthaquinone, and air oxidises 1,4-naphthaquinol, so that the mechanism is similar to that between quinones and aniline[90].

The redox potential of 1,4-naphthaquinone is 0.484 V, whereas those of benzoquinone and of its 2,3-dichloro-5,6-dicyano-derivative are 0.712 and 1.0 V respectively.

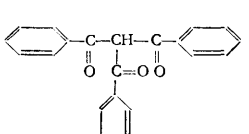
Indane-1,3-dione itself reacts with phenanthraquinone[91] and with nitrophenanthraquinones[92,93] to form 9,9-bis-(1,3-dioxoindan-2-yl)-9,10-dihydro-10-oxophenanthrene and the corresponding nitro-derivative respectively.

V. INTERACTION WITH STABLE RADICALS

The great reactivity of 2-arylindane-1,3-diones towards stable radicals was first observed by Zalukaev and Moiseev[94] in the reaction of diketones with 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2-*p*-methoxyphenyl-2-phenyl-1-picrylhydrazyl[95,96], and 2-*p*-bromophenyl-2-phenyl-1-picrylhydrazyl[21]. With equimolecular proportions of the reactants and an initial concentration of 0.00025 M in toluene at 20°C, the reaction between 2-phenylindanedione and DPPH takes 15–20 s. The reaction of *meta*- and *para*-substituted 2-phenylindanediones with DPPH is equally rapid. This radical detaches the 2-hydrogen atom from the indane ring, as is confirmed by the absence of reaction with 2-methyl-2-phenylindanedione, which does not contain hydrogen in the dione ring. Adding lead dioxide to the 2-arylindanedione system after completion of the reaction regenerates the DPPH radical. Phenyldibenzoylmethane (XII) and tribenzoylmethane (XIII), unlike 2-arylindanediones, do not react with DPPH.

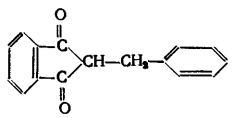


(XII)

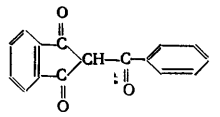


(XIII)

2-Benzyl- and 2-benzoyl-indane-1,3-diones (XIV and XV), in which the dioxoindanyl and phenyl groups are separated by a bridge

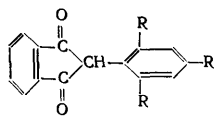


(XIV)



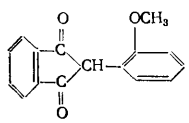
(XV)

also do not react with DPPH under similar conditions. Such diminished reactivity in (XIV) is entirely explicable, since conjugation is considerably weakened by the methylene group[97]. Introduction of an *ortho*-substituent into the phenyl ring produces a sharp decrease in reactivity. No compound of the type

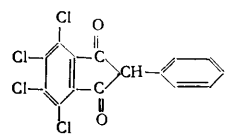


(XVI)
(R=OCH_3, CH_3, C_2H_5, C_3H_7, Br)

reacts either with DPPH or with 2-*p*-methoxyphenyl-2-phenyl-1-picrylhydrazyl in dioxan at 20°C. Even 2-*o*-methoxyphenylindanedione (XVII), which contains one *ortho*-substituent, does not interact with the latter radical. Nevertheless, 4,5,6,7-tetrachloro-2-phenylindanedione (XVIII), which is substituted in the benzene ring of the indanedione system, is highly reactive.

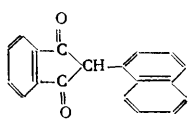


(XVII)

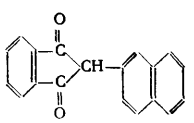


(XVIII)

In order to study the *ortho*-effect[98] a more detailed investigation was made of the reactivity of various substituted indane-1,3-diones—the 2-phenyl (I), 2-*p*-chlorophenyl, 2-*p*-bromophenyl, 2-naphth-1'-yl (XIX), and 2-naphth-2'-yl (XX) derivatives



(XIX)



(XX)

The interaction between 2-arylindanediones and DPPH is a consecutive-parallel reaction:

$$\Phi H + DPPH \xrightarrow{k_1} \Phi\cdot + DPPH - H$$
$$\Phi\cdot + DPPH \xrightarrow{k_2} DPPH - \Phi$$
$$\Phi\cdot + \Phi\cdot \xrightarrow{k_3} \Phi - \Phi$$

Since k_2, $k_3 \gg k_1$, the rate of consumption of DPPH, and hence the rate of detachment of the hydrogen atom from the diketones, are determined by the equation

$$-\frac{d[DPPH]}{dt} = \alpha k_1 [\Phi H][DPPH]$$

where α is the stoichiometric coefficient—the number of radicals that react with one molecule of the dione. The reaction of 2-arylindanediones with DPPH obeys a second-order equation. Table 2 lists the stoichiometric coefficients, the rate constants k_1 of detachment of a hydrogen

atom, activation energies E, and pre-exponential factors k_0 for reaction of the radical with the above compounds in dioxan at 20°C. The activation energy could not be determined for 2-naphth-2'-ylindane-1,3-dione, since it is obviously very small. The values found for the rate constants and activation energies for the 2-arylindanediones are close to those for the corresponding reaction of DPPH with phenols [99-101].

Table 2. Rate constants for the reactions of diphenylpicrylhydrazyl with 2-arylindanediones.

Aryl	a	k_1, M^{-1} min^{-1}	E, kcal $mole^{-1}$	k_0, M^{-1} min^{-1}
Phenyl	1.9	$7.9 \cdot 10^2$	5.5	$1.0 \cdot 10^7$
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Heating 2-phenylindane-1,3-dione with benzoyl peroxide gives the dimer (II), which is obtained also by interaction of the compound with peroxy-radicals formed on the decomposition of azoisobutyronitrile in the presence of oxygen [21]. The ease with which 2-phenylindanedione can be determined colorimetrically in hydrocarbons [106] has enabled it to be tested in the method of inhibitors. The initiator chosen was azoisobutyronitrile, whose decomposition has been thoroughly studied by various methods [107], including the inhibitor method [108]. Fig. 2 illustrates rate curves for the consumption of 2-phenylindanedione at different concentrations in the presence of azoisobutyronitrile in toluene at 80°C and also the time variation of $\lg [\Delta D\infty/(D - D\infty)]$, where D is the optical density of a sample of the reaction mixture withdrawn during the reaction.

Preliminary results showed that, in chlorobenzene under these conditions, 2-phenylindane-1,3-dione is not consumed by reaction with oxygen. The decomposition constants K determined for azoisobutyronitrile by means of 2-phenylindanedione, and also the initiator efficiencies β in toluene and chlorobenzene at 80°C, show complete agreement with values [109] obtained by other methods. It is interesting that unlike known inhibitors—phenols and amines—the stoichiometric coefficient of inhibition for 2-phenylindanedione is in this case unity. Thus the use of 2-arylindanediones to estimate radicals has certain advantages over such inhibitors as 1-naphthylamine and 1-naphthol in view of the simplicity of quantitative control and the definiteness of the conversion products of the inhibitor. Quantitative determination of 2-phenylindanedione and its analogues can be accomplished also spectrophotometrically [110-114], polarographically [115], bromatometrically [116], by anodic volt-amperometric measurements [76], potentiometrically [117], and by other methods [72].

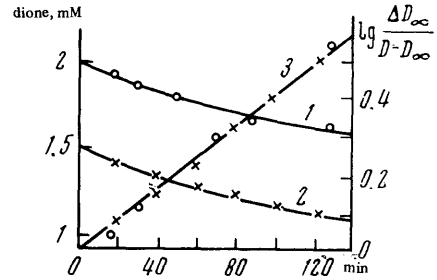


Figure 2. Consumption of 2-phenylindanedione and variation of $\lg [\Delta D\infty/(D - D\infty)]$ with time in experiments on the decomposition of azoisobutyronitrile (0.0005 M) in toluene at 80°C: 1), 2) rate curves; 3) optical density.

VI. 2-ARYLINDANE-1,3-DIONES AS OXIDATION INHIBITORS IN THE LIQUID PHASE

The reaction with radicals such as 2,2-diphenyl-1-picrylhydrazyl suggested that 2-arylindane-1,3-diones would retard the oxidation of alkylarenes by oxygen. An inhibiting effect was shown [118] in the oxidation of *p*-di-isopropylbenzene at 100°C: in the presence of 0.06 mole % of 2-phenylindanedione oxidation was delayed for 25 h. The oxidation of this hydrocarbon is inhibited by 2-*p*-nitro- and 2-*p*-methoxy-phenylindanediones. The causes of the antioxidant power of β-diketones were not elucidated. This problem has been examined in greater detail in a study [21,98] of the oxidation of tetrahydronaphthalene. An active hydrogen atom must be present at the 2-position for inhibiting activity to develop in diketones. Compounds that do not contain such an atom—e.g. 2-ethyl- and 2-methyl-2-phenylindanediones and the dimer of 2-phenylindanedione (II)—do not influence the oxidation. It was found also that the end of the induction period coincided with the instant at which the 2-phenylindanedione was almost completely exhausted. Separate experiments with pure tetralin hydroperoxide in chlorobenzene at 100°C showed that under these conditions decomposition of the hydroperoxide was not affected by 2-phenylindanedione. If a 0.0002 M solution of the latter in tetralin is added before the start of oxidation, an induction period of 100 min is observed.

If the same quantity of this diketone is added during oxidation, no induction period is observed, and the rate of oxidation is almost unchanged. Thus 2-arylindanediones inhibit the autoxidation of hydrocarbons as a consequence of reaction of the active hydrogen atom with peroxy-radicals.

Table 3. Induction periods in the oxidation of tetralin in the presence of substituted indane-1,3-diones.

Substituents	τ, min	Substituents	τ, min
2-Phenyl	100		
2-Naphth-1'-yl	18	4,5,6,7-Tetrachloro-2-phenyl	300
2-Naphth-2'-yl	300		
		2-(2,4,6-Trimethoxyphenyl)	0

A relation has been established between the reactivity of 2-arylindane-1,3-diones towards DPPH radicals and the antioxidant power of the diketones. Thus 2-(2,4,6-trimethoxyphenyl)indanedione (XVI), which does not react with DPPH and the *p*-methoxylated radicals, does not affect the rate of oxidation of tetraline; whereas 4,5,6,7-tetrachloro-2-phenylindanedione, which reacts with these radicals, produces a considerable induction period in the oxidation of tetralin. Table 3 lists the induction periods in the autoxidation of tetralin in the presence of various 2-arylindanediones (0.0002 M) at 100°C. Comparison of the induction period with the behaviour of the 2-arylindanediones towards DPPH shows at least a qualitative parallelism between the antioxidant power of the diketones and the mobility of the 2-hydrogen atom towards the free radical. The lower reactivity of 2-naphth-1'-ylindanedione (XIX) in comparison with 2-phenyl- and 2-naphth-2'-yl-indanedione (XX) is confirmed by its behaviour in the autoxidation of hydrocarbons.

Table 4. Reactivity of phenols.

Compound	k, M^{-1} min^{-1}	τ, min
Phenol	4.3 (19.6°)	75
1-Naphthol	8000 (15.5°)	2250
2-Naphthol	377 (19.0°)	330

It is interesting to draw an analogy between the above compounds and phenols and naphthols. Table 4 lists the rate constants for the reactions of these phenols with DPPH and the induction periods in the oxidation of gasoline in their presence[100]. It is evident that 1- and 2-naphthols are more reactive than phenol in radical reactions. A similar relation should apparently apply to the above 2-arylindanediones. The naphthyl ring system provides greater possibilities for delocalisation of the electron, and the corresponding 2-aryl-1,3-dioxoindanyl radicals should be more stable, so that hydrogen should be more easily detached from diketones containing a naphthyl ring system. However, this is observed only with 2-naphth-2'-ylindanedione: in the case of the naphth-1'-yl derivative the reactivity drops owing to a change in molecular configuration.

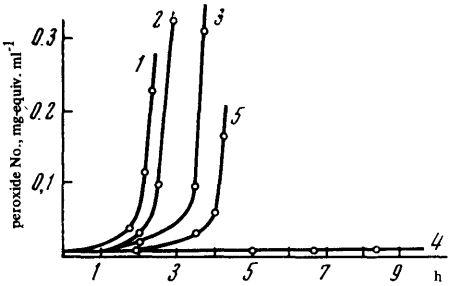


Figure 3. Kinetics of the oxidation of vegetable oil at 120°C in the presence of inhibitors: 1) no antioxidant; 2) 0.01 M ionol; 3) 0.01 M (I); 4) 0.01 M (XXI); 5) 0.001 M (XXI).

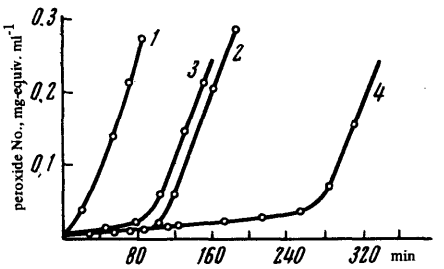
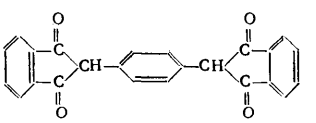


Figure 4. Kinetics of the oxidation of rendered fat at 120°C in the presence of inhibitors: 1) no antioxidant; 2) ionol (0.01 mole kg^{-1}); 3) (I) (0.01 mole kg^{-1}); 4) 2-*p*-hydroxyphenylindanedione (0.01 mole kg^{-1}).

Table 5. Inhibition of the oxidation of sunflower oil at 120°C.

Antioxidant	C, M	τ, min	ε	Antioxidant	C, M	τ, min	ε
None	—	126	—	(XXI)	10^{-2}	>600	19.2
Ionol	10^{-2}	152	1		10^{-3}	186	
(I)	10^{-2}	212	3.3				
				(VII: R = H)	10^{-2}	270	5.5

The antioxidant power of substituted 2-arylindanediones has been examined in detail[119] on the oxidation of sunflower oil and rendered fat. Fig. 3 illustrates the kinetics of oxidation of the oil at 120°C in the presence of equimolar quantities (0.01 M) of ionol, 2-phenylindanedione, and *p*-phenylene-2,2'-bisindane-1,3-dione



(XXI)

Fig. 3 shows that the substituted indanediones are more effective than the well known antioxidant ionol. Compound (XXI) exhibits an inhibiting effect at a concentration of 0.001 M, at which ionol is completely ineffective.

Hydroxylated 2-phenylindanediones, e.g. the *p*-hydroxy-derivative, were highly effective antioxidants for oils and fats. Fig. 4 illustrates the course of the oxidation of rendered fat at 120°C in the presence of ionol, 2-phenylindanedione, and 2-*p*-hydroxyphenylindanedione (each 0.01 mole kg^{-1}). Table 5 lists the induction periods and the efficiencies of certain diketones in the oxidation of sunflower oil. Antioxidant efficiency was calculated[120] by means of the formula

$$\varepsilon = \left(\frac{\tau - \tau_0}{C}\right)_{\text{init}} : \left(\frac{\tau_1 - \tau_0}{C}\right)_{\text{stand}}$$

where τ, τ_1, and τ_0 are the induction periods during oxidation of the substrate in the presence of the test compound and of the standard (ionol) and in the absence of an inhibitor respectively, and C is the inhibitor concentration.

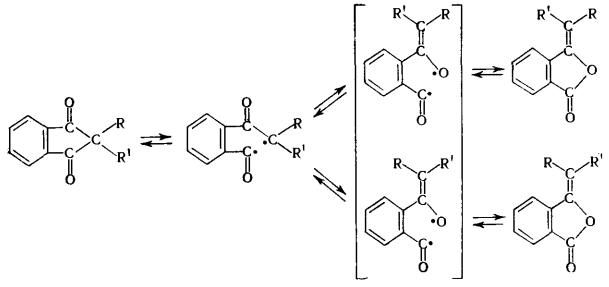
VII. 2-ARYLINDANE-1,3-DIONES AS STABILISERS FOR POLYMERS

The ability of 2-arylindanediones to inhibit the oxidation of hydrocarbons suggested that they could serve as stabilisers for polymers. The efficiency of several substituted 2-phenylindanediones as stabilisers was investigated in polyethylene and polypropylene[121]. Table 6 shows the dependence of the induction period in the oxidation of low-density polyethylene at 150°C on the structure and the concentration of the diketone (the induction period in the oxidation of unstabilised polyethylene is 105 min). The introduction of methoxy- and hydroxy-groups into 2-phenylindanedione enhances the antioxidant efficiency. Unfortunately, these workers[121] did not measure the change in molecular weight of the polymer during aging as a function of the antioxidant, which would have represented the efficiency of the stabiliser most fully and objectively.

Table 6. Dependence of induction period (min) in the oxidation of polyethylene on the structure and concentration of diketones.

Substituted indane-1,3-dione	Concentration, %		
	0.05	0.1	0.5
	induction period		
2-Phenyl	120	180	900
2-*p*-Methoxyphenyl	300	540	990
2-*p*-Hydroxyphenyl	540	840	2040
2-*p*-Chlorophenyl	110	120	780
2-(3,4-Dimethoxyphenyl)	330	570	1080
2-*p*-Dimethylaminophenyl	200	480	640
4-Hydroxy-5-methoxy-2-phenyl	390	660	1680
4,5-Dihydroxy-2-phenyl	490	840	1530
Ionol		610	

This work showed a slight photostabilising effect of substituted 2-phenylindanediones when polyethylene and polypropylene were exposed at 40°C to a PRK-2 lamp. The absorption maxima in the ultraviolet spectra of 2-arylindanediones are situated approximately in the same regions as in the spectra of known photostabilisers, and a most important practical problem is to select effective compounds and study the mechanism of their action[122]. Under the influence of light 2-phenylindanediones may undergo transitions involving keto–enol tautomerism. Light energy may be absorbed also by a different path. Substituted indane-1,3-diones are isomerised by ultraviolet radiation[123–125] into high yields of phthalide derivatives:



Substituted 2-phenylindanediones prevent the thermo-oxidative degradation and cross-linking of Capron [6-polyamide] film and bristle, largely preserving the physico-mechanical properties of these polymers at 200°C and the specific viscosity of the bristle at 150°C. Diketones containing hydroxy-groups in the benzene rings—2-*p*-hydroxyphenylindanedione and 4-hydroxy-5-methoxy-2-phenylindanedione—possess the strongest inhibiting power.

Although 2-phenylindanedione develops its antioxidant properties in saturated polymers (e.g. polyethylene), the effect is almost completely absent in unsaturated rubbers[68], owing to the relatively high reactivity of 2-aryl-1,3-dioxoindanyl radicals. A mixture of 2-phenylindanedione with 1,2,3,4-tetrahydro-2,2,4-trimethylquinoline was found to exert a certain synergic action in the oxidation of SKS-30 rubber[34]. This effect was assessed merely from the time variation in the relative amplitude of the nuclear magnetic resonance signal, without the application of unambiguous methods for proving synergy[129] and measuring the molecular characteristics of the polymer during aging.

Table 7. Induction periods in the oxidation of SKDL rubber in the presence of ionol and of 2-substituted indane-1,3-diones.

Substituent	τ, min.
Ionol	185
Phenyl	7
p-Hydroxyphenyl	24
4'-Hydroxy-3',5'-dimethylphenyl	230
4'-Hydroxy-3',5'-di-isopropylphenyl	34
4'-Hydroxy-3',5'-di-t-butylphenyl	125
3',5'-Diallyl-4'-hydroxyphenyl	50
4'-Hydroxy-3',5'-dimethoxyphenyl	240
3',5'-Dibromo-4'-hydroxyphenyl	20
4'-Oxocyclohexa-2',5'-dienyl	21
3',5'-Dimethyl-4'-oxocyclohexa-2',5'-dienyl	300
No antioxidant	3

p-Hydroxylated 2-arylindanediones (VII) containing a sterically hindered phenolic fragment are of the greatest interest[68] for stabilising unsaturated rubbers. Table 7 gives the induction periods τ in the oxidation of lithium butadiene rubber SKDL at 130°C in the presence of several diketones (VII) and methylenequinones (VIII) at a concentration of 0.02 mole kg^{-1} polymer.

The above results show that several indane-1,3-dione derivatives surpass the well known stabiliser ionol in efficiency of inhibition.

VIII. EFFECT OF 2-ARYLINDANE-1,3-DIONES ON RADICAL POLYMERISATION

In the presence of atmospheric oxygen 2-arylindane-1,3-diones, in contrast to phenols, accelerate the thermal polymerisation[130] of styrene at 100°C. The ability of substituted 2-phenylindanediones to influence the rate of polymerisation is directly related to their reactivity towards the stable radical 2-*p*-methoxyphenyl-2-phenyl-1-picrylhydrazyl: the highly reactive 4,5,6,7-tetrachloro-2-phenylindanedione (XVIII) has a considerable accelerating effect on polymerisation, but the relatively unreactive 2-(2,4,6-trimethoxyphenyl)indanedione (XVI) does not affect its kinetics. The introduction into the *para*-position of an electron-accepting substituent, e.g. a bromine atom, makes the 2-arylindanedione a stronger accelerator of polymerisation; on the other hand, 2-*p*-methoxyphenylindanedione, which contains an electron-donating substituent, has rather less effect than the unsaturated phenyl derivative on the rate of polymerisation. Like many phenols, 2-phenylindanedione does not change the rate of polymerisation in argon[131]. The polymerisation of styrene is actively initiated by the dimer (II), which breaks down into free radicals when heated in hydrocarbons[33]. The formation of polystyrene has been observed[64] also in the arylation of 2-phenylindanedione with diphenyliodonium chloride in the presence of styrene. Radicals of the triphenylmethyl type also accelerate the polymerisation of styrene[132].

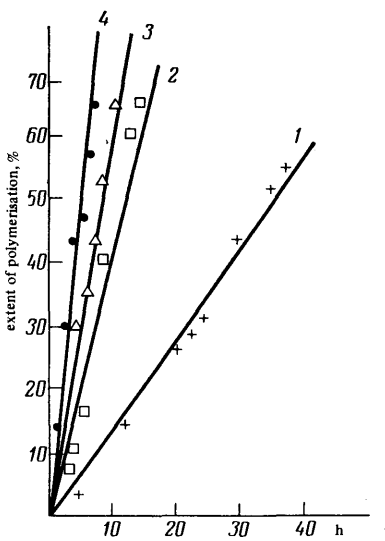


Figure 5. Dependence of rate of polymerisation of SKN-26 rubber on nature and quantity (part by weight) of activator: 1) no activator; 2) 0.2 trihydroxyethylamine; 3) 0.1 (I); 4) 0.2 (I).

The acceleration[133] of emulsion polymerisation in the production of butadiene–nitrile rubbers in the presence of 2-arylindanediones is of practical interest. The use of 0.2 part by weight of 2-phenylindanedione as activator triples the rate of polymerisation observed with the same quantity of trishydroxyethylamine. Fig. 5 illustrates the dependence of the rate of polymerisation on the nature and quantity of activator. In the production of SKN-26 butadiene–nitrile rubber 100% polymerisation is attained in 5 and 20 h respectively in the presence and in the absence of the above quantity of 2-phenylindanedione. The acceleration of emulsion polymerisation is due to the presence of 2-aryl-1,3-dioxoindanyl radicals formed by reaction with the polymerisation initiator—potassium persulphate:

$$2\Phi^- + S_2O_8^{2-} \rightarrow 2\Phi\cdot + 2SO_4^{2-}$$

The formation of dimers of type (II) from 2-arylindanediones has been observed[55] repeatedly in the presence of ammonium persulphate. The increase in the rate of polymerisation of styrene in the presence of 2-arylindanediones in air is also due to radicals resulting[21] from reaction of the β-diketones with oxidation products of styrene.

A second property of 2-arylindanediones of practical importance is their ability to act as chain-transfer agents. Various classes of organic compounds (hydrocarbons, alkenes, thiols, disulphides, amines, phenols, halogenated compounds, etc.) have been investigated[6] in chain-transfer reactions. A few active chain-transfer agents have been widely used in industry under the name regulators or modifiers. In the case of 2-arylindanediones chain transfer can be represented by the scheme

$$RM_n\cdot + \Phi H \xrightarrow{k_s} RM_nH + \Phi\cdot$$
$$\Phi\cdot + M \rightarrow \Phi M\cdot$$
$$RM_n\cdot + M \xrightarrow{k_p} RM_{n+1}\cdot$$

Measurements[134] of chain-transfer constants $C_S = k_S/k_p$ for a series of 2-arylindanediones in the thermal polymerisation of styrene at 100°C were made by Mayo's method[135] from the relation

$$\frac{1}{p} = \frac{1}{p_0} + C_s\frac{[\Phi H]}{[M]}$$

where p_0 and p are the degrees of polymerisation obtained in the absence of a regulator and with a molar ratio $[\Phi H]/[M]$ of regulator to monomer. The results in Table 8 show a fairly wide range of variation—from 0.0001 to 1.05—determined by the structure of the diketone.

Table 8. Chain-transfer constants of 2-substituted indane-1,3-diones.

Substituent	C_s	Substituent	C_s
	0.0044		
Phenyl	0.53	3',4'-Dimethoxyphenyl	0.64
Benzyl	0.058	*p*-Tolyl	0.57
o-Methoxyphenyl	0.01	*m*-Chlorophenyl	0.73
2',4'-Dimethoxyphenyl	0.01	*p*-Chlorophenyl	0.84
		p-Bromophenyl	0.87
2',4',6'-Trimethoxyphenyl	0.0017	3',4'-Dichlorophenyl	1.00
1'-Naphthyl	0.039	3',5'-Dibromophenyl	1.05
2'-Naphthyl	0.65		
p-Methoxyphenyl	0.80	2-Methyl-2-phenyl	0.0001
3',4'-Methylenedioxyphenyl	0.71	2-(3',5'-Dibromophenyl)2-methyl	0.014

Introduction of a phenyl ring into the indane-1,3-dione molecule increases the chain-transfer constant hundredfold, and produces a considerable change in its reactivity. Thus the half-wave potential of anodic oxidation is lowered[75], which is consistent with calculations of the energy of the highest occupied molecular orbital in the anionic form of β-diketones. Separation of the dioxoindanyl ring system

from the phenyl ring by a methylene bridge reduces the chain-transfer constant to one-tenth of its value. The position of the substituent in the phenyl ring has a considerable effect on the reactivity of substituted 2-phenylindanediones, the chain-transfer constants for the *ortho*-substituted 2-*o*-methoxyphenyl-, 2-(2,4-dimethoxyphenyl)-, and 2-(2,4,6-trimethoxyphenyl)-indanediones being far smaller than that for the unsubstituted phenyl derivative. The results[65,123,136] are consistent with the nuclear magnetic resonance spectra: introduction of a phenyl group into indane-1,3-dione increases the chemical shift of the active proton at position 2; introduction of an *ortho*-substituent into 2-phenylindanedione produces a decrease in the chemical shift.

As in the reaction with diphenylpicrylhydrazyl, 2-naphth-1'-ylindanedione (XIX) and 2-naphth-2'-ylindanedione (XX) exhibit different reactivities: (XIX) is less reactive than (XX) and the 2-phenyl compound.

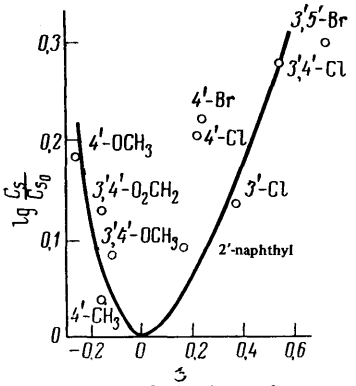
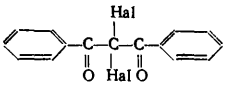


Figure 6. Correlation of chain-transfer constants for substituted 2-phenylindanediones in the thermal polymerisation of styrene, plotted in Hammett coordinates.

It is noteworthy that *meta*- and *para*-substituents in the 2-phenyl ring, independently of whether they are electron-donating or electron-accepting, increase the chain-transfer constant of the compounds in comparison with unsubstituted 2-phenylindanedione. Fig. 6 shows the Hammett plot of the relation obtained. These substituted derivatives have high chain-transfer constants, and surpass several known carriers in activity[6], but are inferior to thiols and certain disulphides[137].

2-Arylindane-1,3-diones containing halogen at position 2 are quite active in chain transfer in the thermal polymerisation of styrene. Compounds of this type have been tested also as modifiers of emulsion polymerisation in the production of polychloroprene[138] and butadiene rubbers[139]. 2-Bromo-2-phenylindanedione (0.6 part by weight) effectively controls the molecular weight of polychloroprene[138] during polymerisation at 50°C. Chain transfer occurs especially efficiently via the bromo-diketone in the initial stages of polymerisation, which is evidently not fortuitous. A disadvantage of 2-halogenated indane-1,3-diones as polymerisation regulators is that the halogen is positive in character[140] and easily detached in weakly alkaline medium, even in sodium hydrogen carbonate solution, for example. They will therefore lose their halogen by this side-reaction during emulsion polymerisation. On the basis of the above researches it has been suggested[141] that dibenzoyldihalogenomethanes



(XXII)

will be more effective regulators of radical polymerisation, free from the above disadvantages.

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The work on the radical reactions of 2-arylindane-1,3-diones examined above shows that β-diketones play an active part in reactions of practical interest. The capacity of substituted indane-1,3-diones for keto–enol tautomerism and the formation of intra- and inter-molecular hydrogen bonds makes this class of compounds attractive for the investigation of radical reactivity. There is every reason to suppose that further study of the radical reactions of 2-arylindanediones will give interesting theoretical and practical results.

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Voronezh Branch,
Lebedev Scientific Research
Institute of Synthetic Rubber

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Advances in the Chemistry of Ethynyl Ketones

R.L.Bol'shedvorskaya and L.I.Vereshchagin

The review deals with problems of the reactivity and the chemical properties of ethynyl ketones. The bibliography includes 201 references.

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I. INTRODUCTION

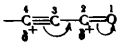
Ethynyl ketones have been attracting increasing interest not only in view of the wide variety of their chemical properties and synthetic possibilities but also owing to their biological activity, particularly their capacity to suppress the growth of various fungi. However, hitherto no reviews have been published on the chemistry of ethynyl ketones with the exception of one [1] on methods of synthesis of these substances. This review is a first attempt at a systematic discussion of the available literature data for the chemical properties of the ketones in which the carbonyl and ethynyl groups are conjugated.

The review covers the periodical literature up to February, 1971.

II. REACTIVITY OF ETHYNYL KETONES

The chemical behaviour of ethynyl ketones is in general determined by the presence in the molecule of three reaction centres—the carbonyl and ethynyl groups and the hydrogen atom involved in the triple bond. The triple bond is known to be less reactive than the double bond in electrophilic addition reactions (addition of halogens, ozone, and peracids [2]) and more reactive in relation to nucleophilic agents (alcohols, amines, thiols, etc.) [2-6].

The reactivity of the ethynyl group in ethynyl ketones is not due solely to the electrophilic properties of the triple bond alone but depends also on the electron-accepting carbonyl group conjugated with it:



As a result 1,2-, 3,4-, and 1,4-addition reactions are characteristic of compounds of this type. Whereas amines, alcohols, and malonic ester add in the 3,4-positions [8-10], hydrazines and semicarbazides (these are much stronger bases and nucleophilic agents than amines) add preferentially in the 1,2-positions. Hydroxylamine, which is a weaker nucleophilic agent than hydrazines and semicarbazides but stronger than amines, can react simultaneously with both electrophilic centres [11].

A wide variety of reactions makes it possible to employ ethynyl ketones as the starting materials for the synthesis of heterocyclic systems. One must note that a particular mode of reaction is determined not only by the basicity of the substance being added but also by the structure of the ethynyl ketone.

III. HYDROGENATION

Depending on the method of hydrogenation, the addition of hydrogen to ethynyl ketones can occur either stepwise with intermediate formation of vinyl ketones and subsequent more far reaching transformation or in a single stage with formation of a reaction product involving the carbonyl group alone. All the methods of hydrogenation of ethynyl ketones described in the literature can be combined in three groups.

1. Catalytic Hydrogenation

Selective hydrogenation of ethynyl ketones depends primarily on the nature of the catalyst. Thus the use of relatively inactive catalysts (colloidal palladium [12], palladium deposited on silica [13] or calcium carbonate [14-17], and Raney nickel [16-18]) makes it possible to stop the hydrogenation process at the stage involving the addition of one mole of hydrogen per mole of the substance hydrogenated. Further saturation with hydrogen leads to the hydrogenation of the double bond and other secondary reactions [19]. The order in which various groups in ethynyl vinyl ketones

of the type $R-CH=CH-CO-C\equiv C-R^1$ (I) are hydrogenated depends mainly on the nature of the substituents R and R^1. The unsubstituted ethynyl vinyl ketone (Ia) and also ethynyl methylvinyl ketone (Ib) are hydrogenated on the $Pd/CaCO_3$ catalyst initially at the triple bond with formation of the divinyl ketone (II) (yield 76%) [20-22]:

$$\underset{\text{(I)}}{R-CH=CH-CO-C\equiv C-R^1} + H_2 \rightarrow \underset{\text{(II)}}{RCH=CH-CO-CH=CHR^1}$$

(Ia, R=R'=H; Iб, R=CH_3, R'=H; Iв, R=H, R'=CH_3)

In the hydrogenation of the ketone (Ic), the first mole of hydrogen adds to approximately equal extents to both triple and double bonds; subsequently $CH_2=CH-CO-CH=CH-CH_3$ (20.6%) and $CH_2=CH-COC_3H_7$ (25.5%) are formed. Moreover, in the first stage, the CO group is also reduced with subsequent isomerisation of the secondary α-ethynylalcohol to the ketone (III):

$$CH_3=CH-CO-C\equiv C-CH_3 \rightarrow \underset{\text{(III)}}{CH_3=CH-CHOH-C\equiv C-CH_3} \rightarrow CH_2=CH-CH=CH-CO-CH_3$$

Isomerisation is observed also in the hydrogenation of disubstituted ethynyl vinyl ketones. Selective hydrogenation of unsubstituted ethynyl vinyl ketone can probably be accounted for by the favourable conditions for the adsorption of the ketone on the catalyst via its triple bond. In this case, steric hindrance results in the reduction of the CO group alone [21].

In the hydrogenation of oct-1-en-3-yn-5-one on $Pd/CaCO_3$, hydrogen adds in the first place to the vinyl group [16]. Unsaturated ketones obtained catalytically have preferentially the *cis*-configuration [16].

2. Chemical Reduction

Ethynyl ketones are readily reduced by nascent hydrogen (zinc + acetic acid) and also by lithium aluminium hydride. The first method is frequently used to reduce the triple bond to a double bond. The reaction takes place in an aqueous alcoholic solution after the addition of catalytic amounts of copper sulphate [23,24]:

$$CH_3-CO-C\equiv C-R \rightarrow \underset{\text{(IV)}}{CH_3-CO-CH=CH-R}$$

$$\rightarrow \underset{\text{(V)}}{R-C\equiv C-C(OH)(CH_3)-C(OH)(CH_3)-C\equiv C-R}$$

(R=CH_3, C_3H_7, C_4H_9)

Together with vinyl ketones (IV), small amounts of ditertiary diethynyl-α-glycols (V) are formed. Aryl-substituted ethynyl ketones are hydrogenated under these conditions to saturated ketones [24]; the vinyl ketones obtained by this method have preferentially the *trans*-configuration.

Lithium aluminium hydride [25] and complexes of the type $Li^+[(RO)_2AlH_2]$ [25,26] reduce ethynyl ketones smoothly to the corresponding ethynylalcohols.

Dibenzoylacetylene (VI) reacts with lithium aluminium hydride in ether or tetrahydrofuran (THF) in different ways at 0-25°C and at −80°C: [27]

$$C_6H_5CHC\equiv C-COC_6H_5 \xleftarrow{-80^\circ} C_6H_5COC\equiv CCOC_6H_5 \rightarrow$$

(VI)

$$\rightarrow C_6H_5-CHC\equiv C-CH-C_6H_5 + \text{(VII)}$$

$$\xrightarrow{0-25^\circ} C_6H_5CHCH=CH=CHC_6H_5 \quad \text{(VII)}$$

$$C_6H_5CHCH_2CH_2CHC_6H_5$$

3. Electrochemical Reduction

The reactivity of ethynyl ketones in electrochemical reduction is determined by the presence of the electron-accepting carbonyl group, which increases the capacity of the triple bond for reduction by an electronic mechanism [28]. Whereas an isolated triple bond combines at a mercury cathode with only one mole of hydrogen, the activated triple bond in diethynyl ketones combines with two moles to form the saturated ketone (VIII): [29,30]

$$(C_6H_5-C\equiv C)_2CO \xrightarrow[\text{Hg cathode}]{H_2} \underset{\text{(VIII)}}{(C_6H_5CH_2CH_2)_2CO}$$

The reduction of disubstituted ethynyl ketones is frequently accompanied by the dimerisation of the vinyl ketone (IX): [30]

$$C_6H_5-CO-C\equiv C-C_6H_5 \xrightarrow{H_2} \underset{\text{(IX)}}{C_6H_5COCH=CH-C_6H_5} \rightarrow C_6H_5COCH=C(C_6H_5)-C_6H_5$$

$$\rightarrow C_6H_5COCH_2-CH(C_6H_5)-C_6H_5$$

The photochemical reduction of 5,5-dimethylhex-3-yn-5-one (X) in isopropyl alcohol has also been described [31]:

$$CH_3-C(CH_3)_2-C\equiv C-CO-CH_3 \xrightarrow[h\nu]{(CH_3)_2CHOH} CH_3-C(OH)(CH_3)-C(OH)(CH_3)-CH_3 + (CH_3)_3C-C\equiv C-C(OH)(CH_3)-CH_3 +$$

(X)

$$+ (CH_3)_3C-C\equiv C-C(OH)(CH_3)-C(OH)(CH_3)-C\equiv C-C(CH_3)_3$$

IV. ADDITION OF HYDROGEN HALIDES

The activated triple bond in ethynyl ketones is capable of combining equally readily with both nucleophilic and electrophilic agents. Whereas the hydrogenation of ethynyl ketones proceeds via consecutive stages involving the addition of initially one and then another mole of hydrogen, the reaction with hydrogen halides terminates in the first stage. The halide ion adds to the β-carbon atom of the triple bond, in agreement with the generally accepted ideas concerning the electron shift in unsaturated ketone molecules [32]. The addition of hydrogen halides to ethynyl ketones usually takes place in chloroform or a mixture of acetic acid and chloroform [33-35]; in some cases, copper(I) chloride was added [33,36]. With strictly equivalent proportions of the starting materials at −40°C, the reaction takes place stereospecifically with formation of the pure *cis*-isomer [34,37,38]. A slight excess of the hydrogen halide or an increase of reaction temperature to 20°C results in the formation either of the sterically pure *trans*-isomer or a mixture of *cis*- and *trans*-isomers (depending on the hydrogen halide used) [34]:

$$p\text{-}R-C_6H_4-CO-C\equiv C-R + HX \xrightarrow{-40^\circ} p\text{-}R-C_6H_4CO-C(X)=C(H)-H$$

$$\xrightarrow{20^\circ} p\text{-}R-C_6H_4CO-C(H)=C(X)-H$$

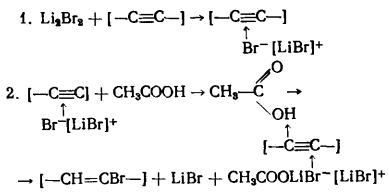
(R=H; OCH_3; Cl
X=Cl; Br, I)

Cis- and *trans*-aryl 2-chloro-1-deuteriovinyl ketones were synthesised under analogous conditions [34]:

$$ArCOC{\equiv}CH + DCl \rightarrow ArCOCD{=}CHCl$$

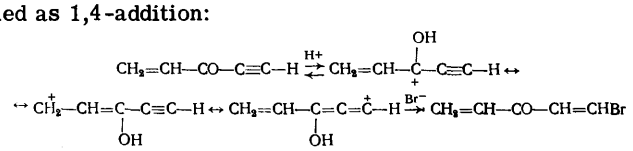
It is believed that the initial reaction stage is nucleophilic attack by the halide ion on the triple bond [34].

Ethynyl ketones are also capable of adding the elements of HBr from LiBr solution in acetic acid [38,39]:



It has been established that the rate of reaction is limited by that of the first stage and depends on the electron-donating properties of the substituents at the triple bond. As the electron-donating properties of the substituent become more pronounced, the reaction rate constant falls, in agreement with the reaction mechanism proposed [39].

In the hydrobromination of the symmetrical ethynyl vinyl ketone, HBr adds to the triple bond only [20,40]. It has been shown [40] that the reaction begins with the protonation of the oxygen atom in the carbonyl group and can be regarded as 1,4-addition:



The reaction takes place stereospecifically in a saturated aqueous solution in the cold with formation of the *cis*-isomer.

V. ADDITION OF HALOGENS

Halogens are added to ethynyl ketones either in ethereal solution [41,42] or in the absence of solvent on heating [37,43]. The reaction with chlorine takes place only when gaseous chlorine is passed through the fused ketone:

$$o\text{-}R{-}C_6H_4{-}C{\equiv}C{-}CO{-}C_6H_5 + X_2 \rightarrow o\text{-}R{-}C_6H_4{-}CX{=}CX{-}CO{-}C_6H_5$$

(R=H, Cl; X=Br, I, Cl)

The addition of a second halogen molecule was not observed under the above conditions.

The bromination of silylethynyl ketones in chloroform leads to a mixture of the *cis*- and *trans*-isomers of $\alpha\beta$-dibromovinyl ketones (XI) (yield 70–75%):

$$R_3SiC{\equiv}C{-}COCH_3 + Br_2 \rightarrow R_3SiCBr{=}CBrCO{-}CH_3$$

(XI)

(R=CH_3, C_2H_5)

When two moles of bromine are allowed to react with the ketone, a mixture of $\alpha\beta$-dibromovinyl ketones and the corresponding tetrabromoketones (yield 15–20%) is formed [44].

Symmetrical ethynyl vinyl ketones are brominated first at the double bond and then at the triple bond with formation of the tetrabromide (XII):

$$R{-}CH{=}CH{-}CO{-}C{\equiv}C{-}R + Br_2 \rightarrow RCHBrCHBrCOC{\equiv}C{-}R \xrightarrow{Br_2} RCHBr{-}CHBr{-}CO{-}CBr{=}CBr{-}R$$

(XII)

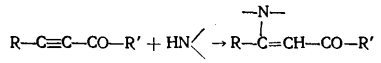
(R=H, CH_3)

This difference between the reactivities of bromine and HBr can be explained by the different site of electrophilic attack owing to the different nature of the attacking reactant. While the hydrobromination reaction is regarded as 1,4-addition with participation of the CO group, the bromination reaction is regarded as 3,4-addition and the authors believe it to be purely electrophilic [20,40].

Ketones of the type $RCOC{\equiv}CCH{=}CH_2$ are brominated non-selectively at the triple and double bonds simultaneously. The comparatively high rate of addition of bromine to the triple bond, which is usually relatively unreactive in relation to bromine, is striking. Evidently the presence of the carbonyl group increases the reactivity of the triple bond, but this influence is difficult to account for if one regards the addition of bromine as an electrophilic addition reaction. It is more likely that, as postulated by Chelpanova et al.[45], nucleophilic addition takes place in the bromination of ethynyl vinyl ketones.

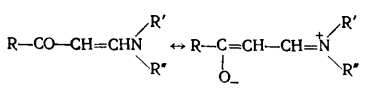
VI. ADDITION OF AMINES

The reaction of amines with ethynyl ketones has been known for a long time. As early as 1904, Watson [46] established that amines add to ethynyl ketones as readily as to vinyl ketones. However, the exact structure of the products was not determined. Somewhat later Andre [47] and then Bowden and coworkers [37,48] and other investigators [49–58] demonstrated that the products of the addition of aliphatic and aromatic amines as well as ammonia to ethynyl ketones have the structure of $\alpha\beta$-unsaturated β-aminoketones (XIII):



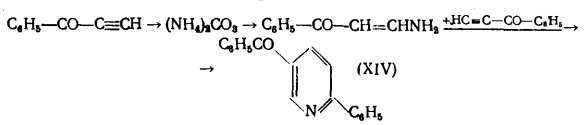
(R=H, Alk, Ar; R'=Alk, Ar) (XIII)

The aminovinyl ketones formed are polarised to a very high degree. As a result of the increase of the negative charge on the oxygen atom and of the positive charge on the nitrogen atom, the dipole moments of the aminovinyl ketone increases sharply [59].



As a result, the reactivity of the double bond relative to nucleophilic agents decreases and a second mole of the amine is not added. Only in a single study by Hoffmann [60], who employed pyrazole and its derivatives as the nucleophilic reactant, diadducts were obtained together with monoadducts. However, the formation of diadducts was demonstrated spectroscopically without their isolation in a pure form.

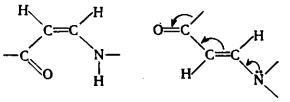
Ethynyl phenyl ketones react with ammonium carbonate in aqueous alcohol to yield pyridine derivatives (XIV): [61,62]



One should note that ethynyl ketones react with amines even at room temperature in the absence of any catalyst in both protic and aprotic solvents. The rate of reaction depends not only on the basicity of the amine [54,58] but also on the structure of the ethynyl ketone involved in the reaction.

The stereochemistry of the addition of amines to ethynyl ketones was studied in only one investigation [63], where it

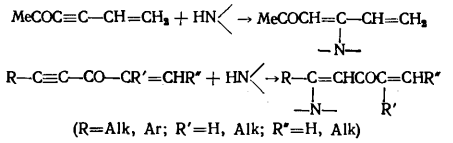
was shown, on the basis of the ^1H NMR data for the reaction mixture, that the reaction of *p*-tolylacetylene with α-phenylethylamine yields the *cis*- and *trans*-isomers of β-(1-phenylethylamino)vinyl-*p*-tolyl ketone [(XV) and (XVI)] with the *cis*-isomer (XV) predominating:



(XV) (XVI)

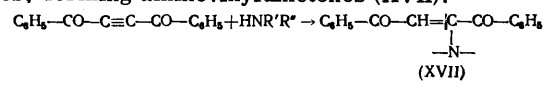
The stability of the *cis*-isomer can be explained by the formation of an intramolecular hydrogen bond [63].

Conjugated ethynyl vinyl ketones combine smoothly with amines at room temperature via the triple bond only [48,64,65]:



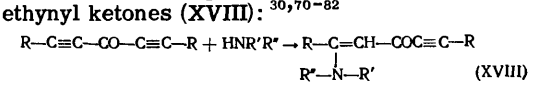
(R=Alk, Ar; R′=H, Alk; R″=H, Alk)

Diketones of the acetylene series readily react with amines, forming aminovinyldiketones (XVII): [66-69]



(XVII)

Aliphatic and aromatic amines add to symmetrical diethynyl ketones of the type R−C≡C−CO−C≡C−R′ preferentially at one triple bond with formation of aminovinyl ethynyl ketones (XVIII): [30,70-82]

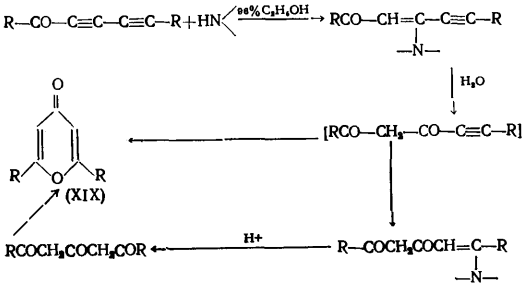


(XVIII)

(R=H, Alk, Ar; R′=R″=H, Alk, Ar)

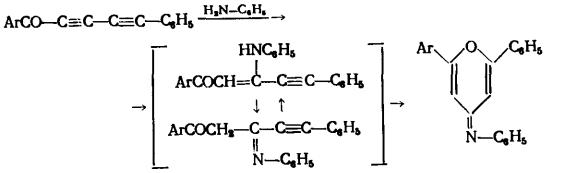
The deactivation of the second triple bond in relation to nucleophilic agents can be explained by the formation of a conjugated system analogous to that in compound (XVI), which evidently greatly weakens the conjugation of the carbonyl group with the second triple bond [80].

The reaction of diacetylenic ketones of the type R−COC≡C−C≡CR′ with secondary aliphatic amines leads to the formation of 2,6-diaryl-4-pyrones (XIX), where R = R′ = Ar: [83]



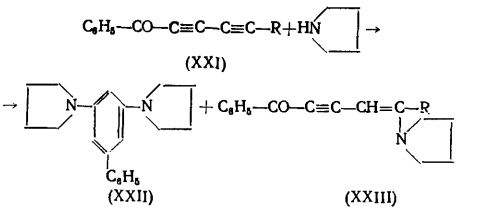
(R=C$_6$H$_5$)

When 1,5-diarylpenta-2,4-diyn-1-ones were allowed to react with aromatic amines, 2,6-diaryl-4-arylaminopyrans (XX) were obtained; it is believed that they are formed via a stage involving the nucleophilic addition of the aromatic amine to the triple bond nearest to the carbonyl group with subsequent cyclisation [83]:



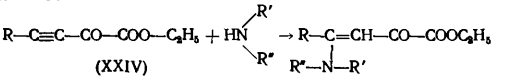
(XX)

On the other hand, treatment of 4-alkyl-1-benzoyldiacetylenes (XXI) with pyrrolidine leads to the formation of diamino-derivatives of biphenyl (XXII) together with the normal addition products (XXIII): [84]



(XXII) (XXIII)

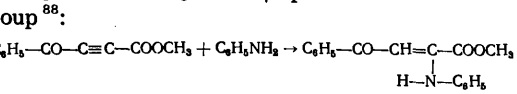
In α-ketoacid esters of the acetylene series (XXIV) containing in the molecule two adjacent electron-accepting molecules, the triple bond is even more reactive with respect to nucleophilic agents. Secondary aliphatic-aromatic amines, morpholine, piperidine [85], as well as primary aromatic amines [86] and aromatic amines containing other functional groups in the ring (aminophenols, aromatic aminoacids, anisidines, and others) [87] readily add to the triple bond of these compounds even at room temperature:

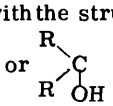


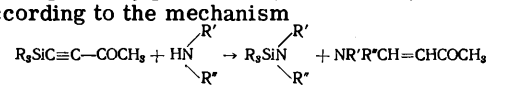
(XXIV)

(R=Alk, Ar; R′=H, Alk, Ar; R″=Alk)

Aniline adds to the triple bond of ketoacids of the type R−CO−C≡C−COO−CH$_3$ in the β-position relative to the keto-group [88]:

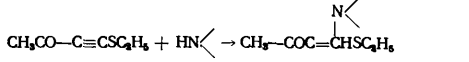


Ethynyl ketones with the structure R−CO−C≡CX, where X = SiR$_3$, SR, NR$_2$, or  are of special interest, since the presence of functional group can alter to some extent the mode of addition of nucleophilic agents to the triple bond. When trialkylsilylethynyl ketones react with methyl- and diethyl-amines, only products the formation of which is probably preceded by the cleavage of the Si−C bond according to the mechanism

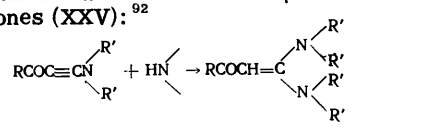


were isolated instead of the expected compounds. On the other hand, the interaction of the ketones investigated with aniline yields the expected anils R$_3$SiC≡C−C(=NC$_6$H$_5$)−CH$_3$. [89]

The addition of amines to ethylthioethynyl ketones R−CO−C≡C−SC$_2$H$_5$ can take place in principle in the 2- and 3-positions. It was found that, as for ethylthiopropiolate esters [90], the addition of an amine to ethylthioethynyl ketones [91] in fact takes place in the 2-position:



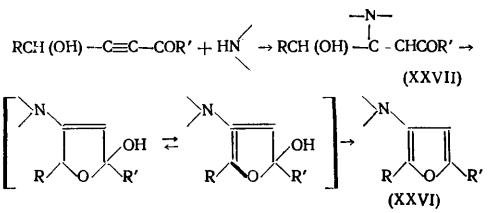
Ethynyl ketones of the type >N−C≡C−CO−R, where the electrophilic properties of the β-carbon atom are greatly enhanced, behave quite differently. The reaction of such ketones with amines at 20°C leads to αβ-unsaturated β-diaminoketones (XXV): [92]



(XXV)

(R=H, Alk; R′=Alk)

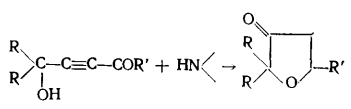
The interaction of secondary α-ethynyl-γ-ketols with primary and secondary amines leads to the formation of β-aminofurans (XXVI): [93]



(XXVII)

(XXVI)

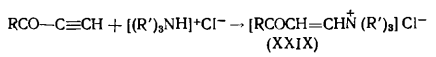
It is believed that initially nucleophilic addition of the amine to the triple bond takes place with subsequent cyclisation of the resulting aminovinylketol (XXVII) to the β-aminofuran (XXVI). When acted upon by secondary amines, tertiary γ-ketols are converted into β-furanones (XXVIII): [93]



(XXVIII)

(R=Alk, R′=Alk, Ar)

Monosubstituted ethynyl ketones react with inorganic salts of tertiary amines, forming quaternary ammonium salts (XXIX) in high yields (87–88%): [94,95]



(XXIX)

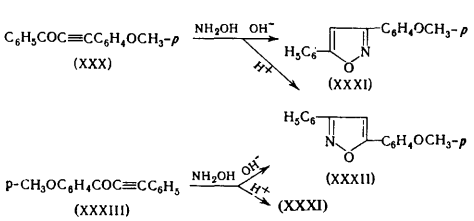
(R=Alk, Ar; R′=Alk)

According to spectroscopic data, the compounds (XXIX) have the *trans*-configuration [95].

VII. ADDITION OF HYDROXYLAMINE, HYDRAZINES, SEMICARBAZIDES, AND OTHER NITROGEN-CONTAINING COMPOUNDS

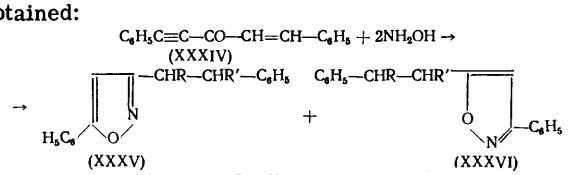
As already mentioned, hydrazines and semicarbazides are stronger bases and nucleophilic agents than amines and therefore they react with ethynyl ketones mainly via the carbonyl group. Hydroxylamine occupies an intermediate position and is therefore capable of attacking simultaneously both reaction centres [11].

Thus the reaction of *p*-anisylbenzoylacetylene (XXX) and other substituted benzoylacetylenes [46,62,96] in an alcoholic alkaline solution proceeds with formation of 3-(*p*-anisyl)-5-phenylisoxazole (XXXI). In an acid medium, the attack on the carbonyl group is facilitated and 5-(*p*-anisyl)-3-phenylisoxazole (XXXII) is formed [11,97]. Directly opposite results were obtained when the starting material was *p*-anisoylphenylacetylene (XXXII):



(XXX) (XXXI) (XXXII) (XXXIII) (XXXI)

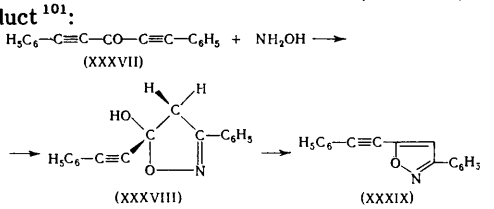
Ferrocenyl-substituted ethynyl ketones [98] and also esters of $\beta\gamma$-acetylenic α-keto-acids [99] and $\alpha\beta$-acetylenic γ-keto-acids [88] behave similarly in the reaction with hydroxylamine. In the reactions with symmetrical disubstituted ethynyl vinyl ketones (XXXIV), the formation of isoxazole derivatives is accompanied by the subsequent addition of a second hydroxylamine molecule to the double bond and, depending on the reaction conditions, the isomeric isoxazoles (XXXV) [100] and (XXXVI) [101] can be obtained:



(XXXIV) (XXXV) (XXXVI)

(a) R=NHOH, R′=H; (b) R=H, R′=NHOH)

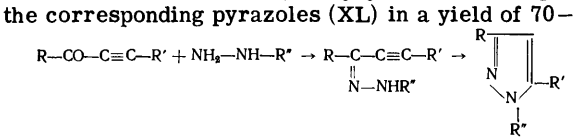
The reaction of 1,5-diphenylpenta-1,4-diyn-3-one (XXXVII) with hydroxylamine in an aqueous alcoholic solution involved the formation of Δ^2-isoxazoline (XXXVIII) as the only product [101]:



(XXXVII) (XXXVIII) (XXXIX)

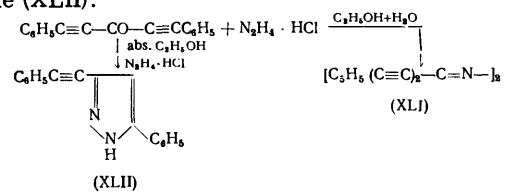
Prolonged heating of the isoxazoline (XXXVIII) in xylene or an aqueous alcoholic solution with distillation of water yields 3-phenyl-5-phenylethynylisoxazole (XXXIX).

In most cases the interaction of hydrazines with ethynyl ketones proceeds via the carbonyl group. Mono- [62,92,98] and di-substituted [62,96,98,101,102] ethynyl ketones and α-diketones [68,98] as well as γ-ethynyl-α-ketols [103] give rise to the corresponding pyrazoles (XL) in a yield of 70–80%:



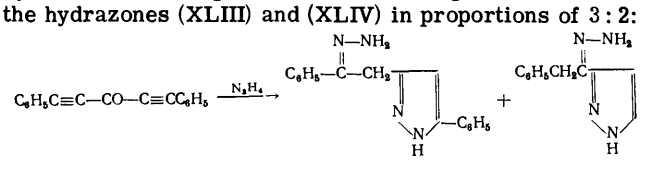
(R = H, Alk, Ar, —COOR; R′=H, Alk, Ar, —COC_6H_5, —C(OH)<, —N(R)$_2$)

Depending on the experimental conditions, the reaction of 1,5-diphenylpenta-1,4-diyn-3-one with hydrazine hydrochloride gives two different products. In aqueous ethanol solution, the azine (XLI) is formed, while in absolute ethanol the product is 3(5)-phenyl-5(3)-phenylethynylpyrazole (XLII): [101]



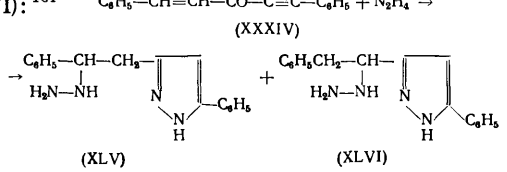
(XLI) (XLII)

1,5-Diphenylpenta-1,4-diyn-3-one reacts with an excess of hydrazine in boiling absolute alcohol to give a mixture of the hydrazones (XLIII) and (XLIV) in proportions of 3:2:



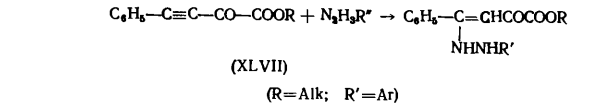
(XLIII) (XLIV)

The interaction of 1,5-diphenylpent-1-en-4-yn-3-one (XXXIV) with anhydrous hydrazine in absolute alcohol gives rise to a mixture of the pyrazoles (XLV) and (XLVI): [101]



(XXXIV) (XLV) (XLVI)

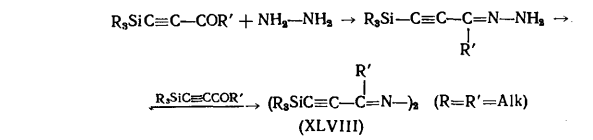
In contrast to the ethynyl ketones discussed above, esters of phenylethynylglyoxalic acids (XLVII) react with hydrazine derivatives and aromatic acid hydrazides according to the same mechanism [99] as with amines:



(XLVII)

(R=Alk; R'=Ar)

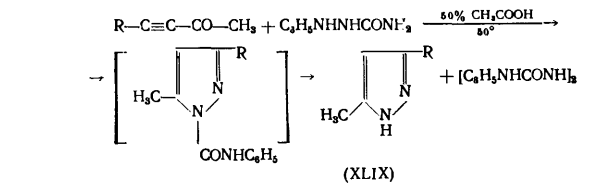
When trialkylsilylethynyl ketones react with hydrazine, the products are not pyrazoles but hydrazones, which are converted in the presence of an excess of the ketone into the azines (XLVIII): [44]



(XLVIII)

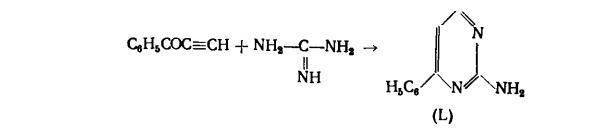
The reaction of silylethynyl ketones with 2,4-dinitrophenylhydrazine and 3,5-dinitrobenzoylhydrazine terminates in the hydrazone stage. The hydrazones obtained do not cyclise with the corresponding pyrazoles under the influence of acetic anhydride and acetic acid and char under these conditions [104]. Thus the trialkylsilyl group in the α-ethynylhydrazones is in fact an obstacle to their cyclisation.

In the reaction with ethynyl ketones, semicarbazides behave like hydrazines. Thus phenylsemicarbazide gives rise to pyrazoles (XLIX): [105]



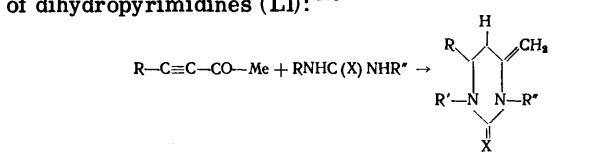
(XLIX)

The only product of the condensation of guanidine with ethynyl phenyl ketone is 2-amino-4-phenylpyrimidine (L): [62]



(L)

Urea and thiourea derivatives react with ethynyl ketones in ethereal solution in the presence of concentrated sulphuric acid to give the corresponding derivatives of dihydropyrimidines (LI): [106]



(LI)

(R=Alk; R'=Alk, Ar; R''=Alk; X=O, S)

VIII. ADDITION OF ALCOHOLS, PHENOLS, THIOLS, AND THIOPHENOLS

Whereas the addition of amines to the activated triple bond of ethynyl ketones takes place readily in the absence of catalysts even at room temperature, the addition of alcohols is possible only in the presence of a basic catalyst. The reaction with terminal ethynyl ketones does not stop at the stage involving the addition of one mole of the alcohol but continues until the formation of the acetal of the corresponding β-ketoaldehyde (LII) (yield 60–75%) [37,97]:

(LII)

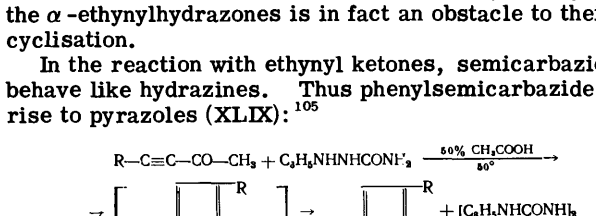
(R=Alk, Ar; R'=Alk)

The reaction was carried out in the presence of sodium alkoxide at 0–5°C. [107] The formation of alkoxyvinyl ketones was not observed under these conditions. Primary, and secondary alcohols add to disubstituted ethynyl ketones in the presence of both alkoxides [9,37,108–110] and tertiary amines [110] with the exclusive formation of the monoadducts (LIII):

(LIII)

(R=Alk, Ar; R'=Alk, Ar)

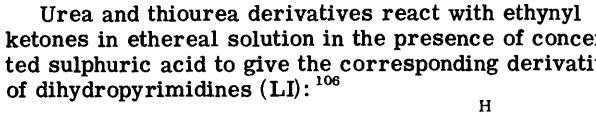
The addition of alcohols to phenylbenzoylacetylene in the presence of potassium hydroxide takes place with the cleavage of the initial ketone to acetophenone and potassium benzoate [110]. It is interesting that alcohols add in the presence of BF_3 as the catalyst. Thus dibenzoylacetylene reacts with alcohol in the presence of BF_3, yielding 3-alkoxy-2,5-diphenyldihydrofuranone (LIV) as the sole product [111]:



(LIV)

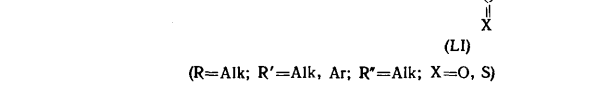
One should note that the addition of alcohols to ethynyl ketones is stereospecific like the addition of amines [33,112,114]. For example, the reaction of isopropyl methylethynyl ketone with methanol in aqueous potassium carbonate solution yielded a pure $\alpha\beta$-unsaturated *cis*-β-methoxyketone, which did not isomerise under the reaction conditions.

The reaction of cyclo-oct-2-ynone with deuteriated aqueous methanol in the presence of potassium carbonate gives 2-deuterio-3-methoxycyclo-oct-2-enone (LV) containing a small admixture (less than 10%) of the non-deuteriated product [113]. There is no doubt about the *cis*-configuration of compound (LV):



(LV)

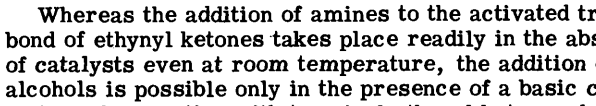
The addition of phenols to ethynyl ketones in the presence of sodium phenoxide [37] or pyridine [114] takes place sluggishly and always results in the formation of a monoadduct:



(R=H, Ar; R'=Ar)

In the reaction with alcohols and phenols under analogous conditions, silylethynyl ketones are cleaved at the Si–C bond [89].

Thiols and thiophenols add similarly to alcohols and phenols, and in both cases only the monoadducts were isolated [33,37,112,113]:



(R=H, Alk; R', R''=Alk, Ar)

The reaction takes place at room temperature in the presence of alkali metal alkoxides [37,112,113], alkali, and in a few cases also in the absence of the catalyst [65]. Thiols add to symmetrical ethynyl vinyl ketones at the triple bond in the first place and then at the double bond [65]:

$$R{-}CH{=}CH{-}CO{-}C{\equiv}CH + RSH \rightarrow RCH{=}CH{-}COCH{=}CHSR + RCH(SR)CH_2{-}CO{-}CH{=}CHSR$$

The study of the stereochemistry of the addition of thiols and thiophenols to ethynyl ketones showed that the reaction is rigorously stereospecific and takes place in accordance with the *trans*-addition rule, yielding the *cis*-adducts only [37,112,113].

IX. ADDITION OF ACIDS

As with amines, alcohols, and thiols, the addition of acids to ethynyl ketones is a nucleophilic process; the anionoid fragment of the acid is directed towards the β-carbon atom of the multiple bond. The addition of an arenesulphonic acid to the triple bond of ethynyl ketones was first described by Kohler and Barrett [115], who treated benzoylphenylacetylene with toluene-*p*-sulphonic acid and isolated two stereoisomeric sulphones (LVI). Somewhat later Bowden et al. [37] obtained similar results in the reaction of ethynyl phenyl ketone with the same sulphonic acid:

$$\underset{(R=H,\ C_6H_5)}{C_6H_5COC{\equiv}CR} + p\text{-}CH_3C_6H_4SO_2H \rightarrow \underset{cis\text{- and }trans\text{-}}{C_6H_5COCH{=}C(R){-}SO_2C_6H_4{-}CH_3\text{-}p} \quad (LVI)$$

The addition of acetic and benzoic acids to ethynyl phenyl ketone in the presence of basic catalysts takes place fairly smoothly and yields the acetate (LVIIa) and the benzoate (LVIIb) respectively, which are mixtures of the *cis*- and *trans*-isomers [116]:

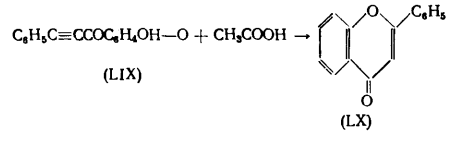
$$C_6H_5COC{\equiv}CH \xrightarrow[RCOOH]{RCOONa} C_6H_5COCH{=}CHOCOR \ (LVII)$$

$$C_6H_5COC{\equiv}CH \xrightarrow[N(C_2H_5)_3]{CH_3COOH} C_6H_5COCH_2CH(OCOCH_3)_2 \ (LVIII)$$

(a) R=CH_3; (b) R=C_6H_5

Treatment of ethynyl phenyl ketone with an excess of acetic acid in the presence of triethylamine yields the diacetate (LVIII).

The addition of acetic acid to 3-(*o*-hydroxyphenyl)-1-phenylprop-1-yn-3-one (LIX) in the presence of polyphosphoric acid at 100°C leads to the flavone (LX): [117]



(LIX) (LX)

The reaction of hydrogen selenide and also of selenols with ethynyl phenyl ketone takes place successfully without a solvent and a catalyst and also in ether in the presence of catalytic amounts of pyridine. The yield of selenovinyl ketones (LXI) reaches 60–80%: [118]

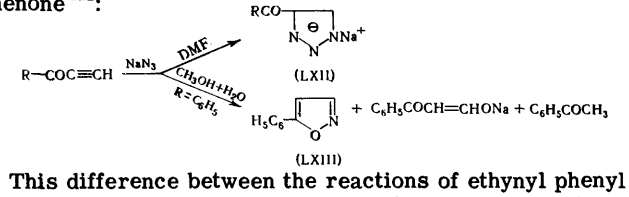
$$RCOC{\equiv}CH + RSeH \rightarrow \underset{(LXI)}{RCOCH{=}CH{-}SeR}$$

In contrast to the acids discussed above, the addition of diesters of phosphorous and phosphorothious acids to ethynyl ketones takes place only at the carbonyl group without involving the C≡C bond [119,120]:

$$R'COC{\equiv}CR'' + (RO)_2PH \xrightarrow{RONa} (RO)_2P(X){-}CR'(OH){-}C{\equiv}C{-}R''$$

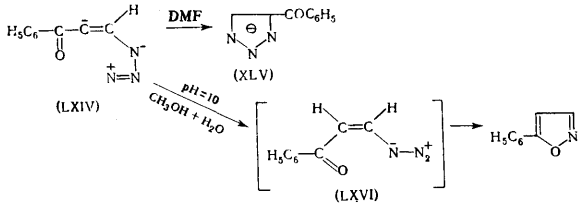
(X=O, S)

The reaction of ethynyl ketones with sodium azide, investigated by Nesmeyanov and Rybinskaya [121,122], which leads to the formation of either triazoles or isoxazoles depending on the reaction conditions, occupies a special place. Thus ethynyl propyl or ethynyl phenyl ketone reacts with sodium azide in dimethylformamide (DMF) to give the corresponding triazole (LXII). [121] On the other hand, the reaction of ethynyl phenyl ketone with NaN_3 in a proton-donating solvent proceeds with formation of 5-phenylisoxazole (LXIII) and a small admixture of the sodio-derivatives of benzoylacetaldehyde and acetophenone [122]:



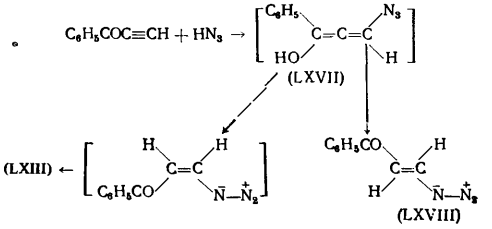
(LXII) (LXIII)

This difference between the reactions of ethynyl phenyl ketone with the azide ions in DMF and a protic solvent can be accounted for by a change in the conditions governing the stabilisation of the carbanion (LXIV) formed as a result of the nucleophilic attack by the azide ion on the triple bond. It is suggested that in aprotic solvents the lifetime of the carbanion (LXVII) is long enough for its cyclisation to the stable triazolyl anion system (LXV):



(LXIV) (XLV) (LXVI)

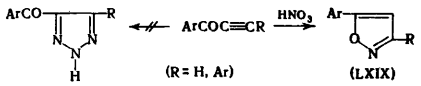
In proton-donating solvents, this carbanion can be protonated, which apparently results in the formation of an unstable intermediate—*cis*-β-azidovinyl phenyl ketone (LXVI), which, owing to the favourable disposition of the carbonyl and azide groups, is converted into the stable heterocyclic system of 5-phenylisoxazole with evolution of nitrogen. However, one cannot rule out the possibility that at low pH ethynyl phenyl ketone reacts with HN_3 to give a 1,4-addition product, from which a mixture of the *cis*- and *trans*-isomers [(LXVII) and (LXVIII) respectively] of azidovinyl phenyl ketone is formed as a result of a prototropic rearrangement:



(LXVII) (LXIII) (LXVIII)

trans-β-Azidovinyl phenyl ketone is quite stable under the usual conditions and can be isolated, while the *cis*-form is unstable and decomposes spontaneously with formation of 5-phenylisoxazole (LXIII).

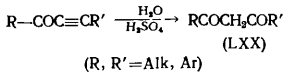
Ethynyl ketones react with NH_3 in chloroform to form isoxazoles (LXIX) and not triazoles [123]:



(R = H, Ar) (LXIX)

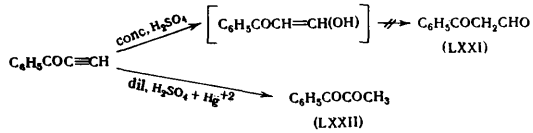
X. HYDRATION

The addition of water to disubstituted ethynyl ketones has been known for a long time. As early as 1899, Nef [41] obtained dibenzoylmethane by treating benzoylphenylacetylene with concentrated sulphuric acid. This method has been used in many other investigations [47,108,109,124-126] and regardless of the nature of the substituent led in all cases to β-diketones (LXX):



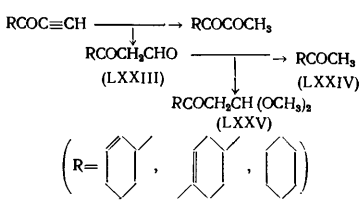
(R, R′ = Alk, Ar)

Monosubstituted ethynyl ketones are not hydrated in concentrated sulphuric acid; in dilute sulphuric acid, the reaction proceeds only on heating in the presence of mercury salts with formation of α-diketones (LXXII) instead of the expected α-ketoaldehydes (LXXI): [37]

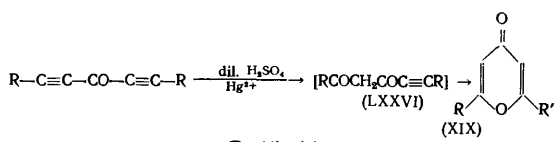


(LXXI) (LXXII)

However, the study of the reactivities of compounds of the Δ^3-cyclohexane series showed that, together with the main products, which are α-diketones, the isomeric β-ketoaldehydes (LXXIII) as well as their conversion products—the methyl ketones (LXXIV) and acetals (LXXV)—are nevertheless formed in comparatively small amounts [127]:

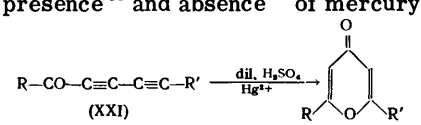


The products of the hydration of symmetrical ethynyl ketones in dilute sulphuric acid on heating in the presence of mercury salts are γ-pyrones (XIX): [70,75,128]



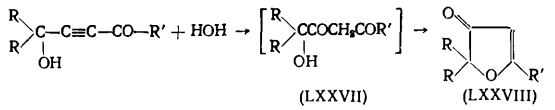
(R = Alk, Ar)

Probably water adds to one triple bond with formation of the intermediate ketone (LXXVI), which then cyclises to (XIX). Similar results were obtained in the hydration of asymmetric diacetylenic ketones (XXI) by dilute sulphuric acid in the presence [83] and absence [84] of mercury salts:



(XXI) (R = C_6H_5; R′ = Alk, Ar)

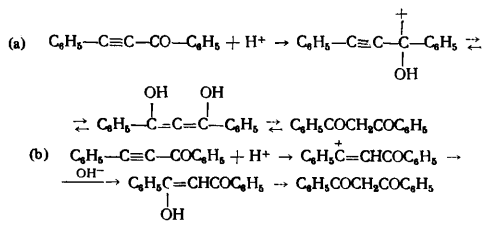
α-Ethynyl-γ-ketols are fairly readily hydrated in dilute sulphuric acid and in an alkaline alcoholic medium in the presence of mercury salts as well as in the presence of amines in protic solvents [93,103], being converted under these conditions into β-furanones (LXXVIII) in 80–90% yield via the β-diketol (LXXVII) stage. In aqueous dioxan, the yield of furanone is scarcely 50%:



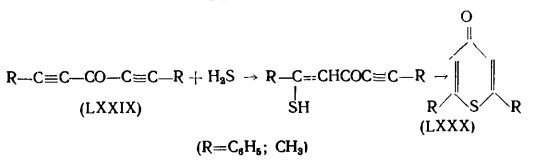
(LXXVII) (LXXVIII)

The addition of water to dibenzoylacetylene in the presence of mercury salts in an acid medium and in the presence of aliphatic amines in an aqueous alcoholic solution results in the formation of 1,4-diphenylbutane-1,2,4-trione [68].

By analogy with the available literature data for the mechanism of the hydration of unsaturated acids [129] and ketones [130-132], two possible mechanisms have been proposed [133] for the hydration of ethynyl ketones in an acid medium:



In the first case, the rate-limiting stage of the process is probably the transformation of the phenylbenzoylacetylene oxonium salt and in the second case a proton adds to phenylbenzoylacetylene. Having measured the rate constants for the hydration of ethynyl ketones of different basicities, Noyce and Debruin [133] showed that the hydration of phenylbenzoylacetylene proceeds via a stage involving proton transfer from the acid medium to the α-carbon atom of the triple bond [i.e. via mechanism (b)]. Probably the interaction of symmetrical diethynyl ketones (LXXIX) with hydrogen sulphide can be interpreted likewise. The reaction in absolute ethanol takes place with formation of 2,6-disubstituted thio-γ-pyrones (LXXX): [128,134]



(LXXIX) (LXXX)

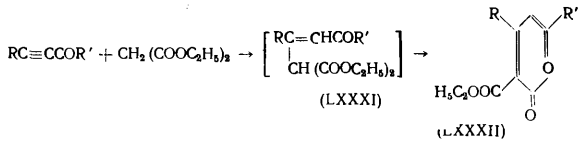
(R = C_6H_5; CH_3)

XI. MICHAEL CONDENSATION AND RELATED REACTIONS

The most typical property of ethynyl ketones is their capacity to undergo the Michael condensation with compounds containing active methylene groups. The nucleophilic agents can be not only carbonyl and carboxylated substances of the type $O{=}\overline{C}{-}CH_2{-}\underset{|}{C}{=}O$, but also the corresponding nitriles, nitro-compounds, and sulphones.

The interaction of ethynyl ketones with malonic ester has been investigated in greatest detail. By analogy with the reactions discussed above, it might have been expected that ethynyl ketones involved in the Michael condensation would form $\alpha\beta$-unsaturated ketones. However, in most

cases cyclisation products—derivatives of α-pyrones (LXXXII)—were isolated and not the open-chain compounds (LXXXI):[10,135-138]

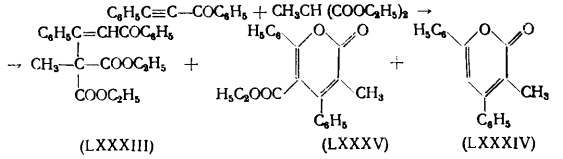


(LXXXI) (LXXXII)

The interaction of ethynyl ketones with malonic ester has been suggested[10] as a method for their identification. However, in studies on ethynyl furyl ketones, it was found that the reaction is not general[139].

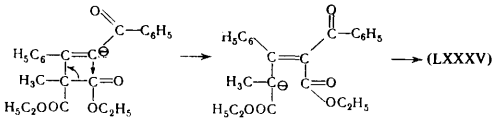
Michael condensation involving ethynyl ketones took place smoothly in an alcoholic medium in the presence of traces of the corresponding sodium alkoxides. When the reaction is carried out in the presence of an equimolar amount of sodium alkoxide or metallic sodium, its course changes. Thus the reaction of diethyl methylmalonate with phenylbenzoylacetylene yields under these conditions the "normal" adduct—4,4-diethoxycarbonyl-1,3-diphenylpent-2-en-1-one (LXXXIII) together with 3-methyl-4,6-diphenyl-2-pyrone (LXXXIV) and ethyl 3-methyl-4,6-diphenyl-2-pyrone-5-carboxylate (LXXXV).[140]

Compound (LXXXIV) is a product of the decarboxylation of the ester (LXXXIII) or (LXXXV):

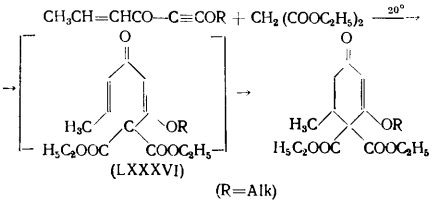


(LXXXIII) (LXXXV) (LXXXIV)

It is suggested that the pyrone (LXXXV)—the "anomalous" reaction product—is formed from the "normal" adduct (LXXXIII) according to the following mechanism:



The interaction of malonic ester with the ethynyl vinyl ketone $CH_3CH{=}CHCOC{\equiv}COR$ in absolute t-butyl alcohol in the presence of catalytic amounts of potassium t-butoxide involves the formation of the intermediate open-chain product (LXXXVI) which subsequently cyclises as follows:

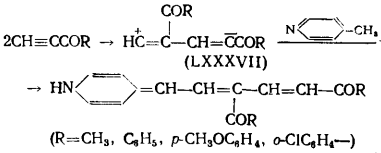


(LXXXVI)

(R=Alk)

The antibiotic griseofulvin was obtained from ethynyl vinyl ketones and coumaranone via this reaction[124].

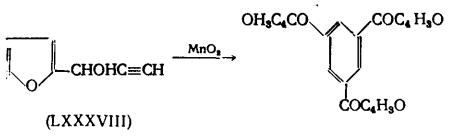
The intermediate formation of the zwitter-ion (LXXXVII) in reactions of ethynyl ketones with γ-picoline and related compounds has been postulated[141]:



(LXXXVII)

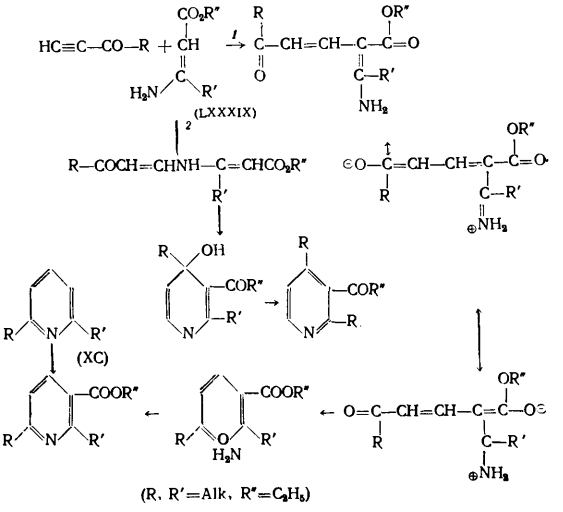
(R=CH_3, C_6H_5, p-$CH_3OC_6H_4$, o-ClC_6H_4—)

Probably ethynylfurylmethanol (LXXXVIII) reacts similarly under the influence of activated manganese dioxide[142]:



(LXXXVIII)

An interesting reaction of ethynyl ketones with esters of α-aminovinylcarboxylic acids (LXXXIX) has been described[61]:



(LXXXIX) (XC)

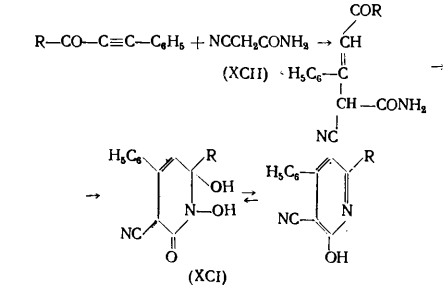
(R, R'=Alk, R"=C_6H_5)

In principle, this reaction can proceed via a mechanism of the type of Michael condensation (*1*) and via a pathway (*2*), where the amino-group adds to the activated C≡C bond. The study of the physical and chemical properties of the final reaction products [pyridine derivatives (XC)] demonstrated unambiguously that the reaction has mechanism (*1*).

The low probability of the addition of the amino-group of aminovinyl ketones to the triple bond of ethynyl ketones can be accounted for by the reduced basicity of the amino-group owing to the conjugation of the lone electron pair of the nitrogen atom with the carbonyl group[143].

Pyrroles and indoles, which have similar structures, react with ethynyl ketones via the hydrogen atom in the α- or β-position in the ring[141].

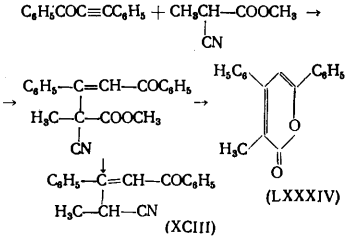
Another characteristic instance of this type of condensation is the formation of pyridones (XCI) by the reaction of ethynyl ketones with cyanacetamide (XCII):[137,144]



(XCII) (XCI)

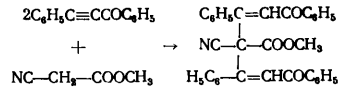
The reaction of phenylbenzoylacetylene with ethyl phenylacetate yielded 3,4,6-triphenyl-2-pyrone[145], while the reaction with methyl α-cyanopropionate in the presence

of an excess of sodium alkoxide gave the α-pyrone (LXXXIV) and a small amount of the unsaturated nitrile (XCIII):[115]



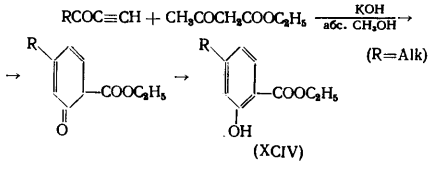
(XCIII) (LXXXIV)

Methyl α-cyanoacetate reacts with phenyl benzoylacetylene via the mechanism



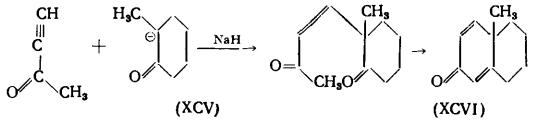
A change in the ratio of the initial reactants does not affect the course of the reaction[115].

The condensation of unsubstituted ethynyl ketones with acetoacetic ester takes place quite differently. The final product of this reaction is a derivative of ethyl salicylate (XCIV):[146]



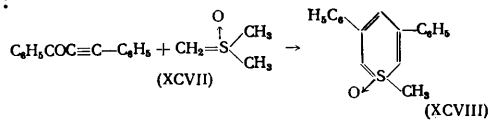
(XCIV)

The addition of methylcyclohexanone (XCV) to ethynyl methyl ketone in the presence of sodium hydride proceeds via a stage of internal aldol condensation with subsequent dehydration and formation of 10-methyl-2-oxo-Δ 1,9;3,4-hexahydronaphthalene (XCVI):[147]



(XCV) (XCVI)

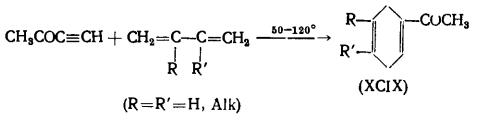
An example of the condensation of ethynyl ketones with compounds containing an active methylene group is provided also by the reaction of phenylbenzoyl acetylene with dimethyloxosulphonium methylide (XCVII), which takes place in dimethyl sulphoxide solution at 20°C with formation of 1-methyl-3,5-diphenylthiabenzene-1-oxide (XCVIII):[148]



(XCVII) (XCVIII)

XII. DIELS-ALDER SYNTHESIS

Ethynyl ketones are extremely active dienophiles in Diels-Alder synthesis. Thus butynone, the simplest ethynyl ketone, reacts readily at 50–120°C with butadiene and many of its homologues (isoprene, piperylene, dipropenylene, and di-isopropenylene), yielding dihydrobenzophenones (XCIX):

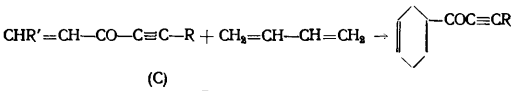


(R=R'=H, Alk) (XCIX)

Ethynyl propyl ketone and ethynyl phenyl ketone enter into a Diels-Alder reaction with butadiene under similar conditions[149,150]. The reactivity of disubstituted ethynyl ketones in this process is somewhat lower[22,100,151].

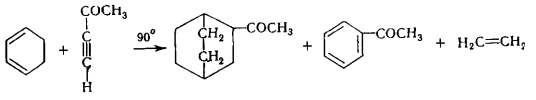
The condensation of ethynyl methyl ketone with chloroprene, bromoprene, and 1-chlorobutadiene at 80–125°C in benzene solution gave high yields of the corresponding halogenodihydrobenzophenones[152,153].

Petrov and coworkers[20,154], showed that in the reactions between butadiene and isomeric hex-2-en-5-yn-4-one and hex-1-en-4-yn-3-one (C, b) the process involves the unsubstituted multiple bond, preferentially in the first case and exclusively in the second, regardless of its nature. The addition of butadiene to pent-1-en-4-yn-3-one (C, a) and hept-2-en-5-yn-4-one takes place exclusively at the double bond:

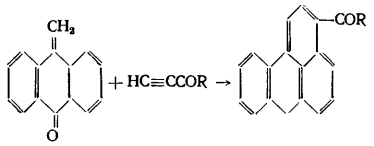


(C)
(a) R=H; (b) R=CH₃

Ethynyl ketones react fairly readily with cyclopentadiene[150,155,156]. The condensation with cyclohexa-1,3-diene takes place with greater difficulty and is accompanied by the splitting off of the endoethylene bridge with formation of acetophenone and ethylene[155]:



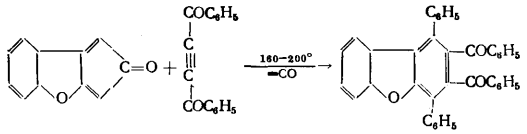
On heating in acetic acid solution, ethynyl ketones condense with methyleneanthrone (CI), the final product being 3-substituted mesobenzanthrones (CII):[157]



(CI) (CII)

Dibenzoylacetylene, which readily condenses with dienes in ether or dioxan, is used as a dienophile similarly to ethynyl monoketones[18,158].

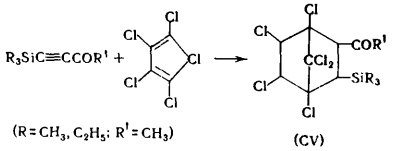
"Indanocyclone" (CIII) reacts with dibenzoylacetylene in ethyl acetate at 160–200°C to form 1,4-diphenyl-2,3-dibenzoylfluorenone (CIV):[159]



(CIII) (CIV)

The condensation of diacetylacetylene with butadiene could not be achieved, since the initial diacetylacetylene decomposed under the reaction conditions[160].

Silylethynyl ketones do not react with cyclopentadiene [161], probably owing to the deactivation of the critical bond under the influence of a_π-p_π-conjugation with the silicon atom. However, these studies show at the same time that silylethynyl ketones condense with hexachlorocyclopentadienone at 150–180°C with formation of hexachlorosilylbicycloheptadienyl ketones (CV) in a yield of 15–30%: [161]

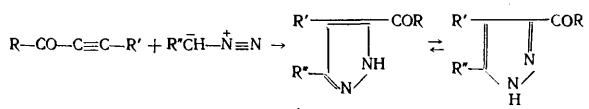


(R = CH_3, C_2H_5; R' = CH_3) (CV)

XIII. ADDITION OF 1,3-DIPOLAROPHILES

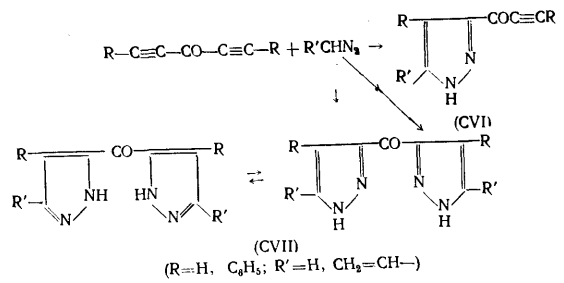
1. Addition of Diazoalkanes

Ethynyl ketones react fairly readily with diazoalkanes, which are powerful nucleophilic agents. The reaction is general for ethynyl ketones and is regarded as dipolar 1,3-addition to the triple bond [62,162–167]:



(R = Alk, Ar; R' = H, Alk, $-COOCH_3$; R'' = H, CH_2=CH–, CH_3)

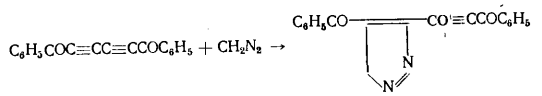
Ketones of the type RC≡CCOC≡CR react with diazoalkanes to form 1 : 1 and 1 : 2 adducts [(CVI) and (CVII) respectively] [163,168]:



(CVII)

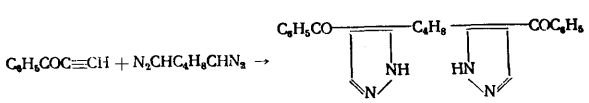
(R = H, C_6H_5; R' = H, CH_2=CH–)

Diazomethane adds to 1,6-diphenylhexa-2,4-diyne-1,6-dione (CVIII) at only one C≡C bond with formation of 4-benzoyl-3(5)-benzoylethynylpyrazole (CIX): [168]



(CVIII) (CIX)

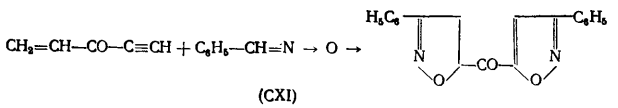
Bisdiazohexane (CX) reacts with benzoylacetylene as follows [169]:



(CX)

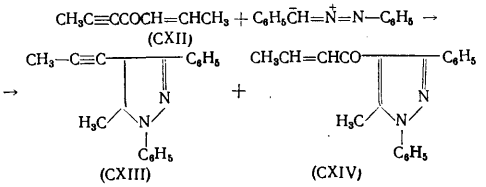
2. Addition of Nitrile *N*-Oxides

Like diazoalkanes, nitrile *N*-oxides and nitronic esters react with ethynyl ketones according to the dipolar 1,3-addition mechanisms. Benzonitrile *N*-oxide (CXI) add to unsubstituted ethynyl vinyl ketones at both multiple bonds [170]:



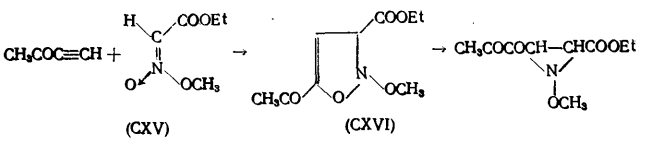
(CXI)

In the interaction of monosubstituted ethynyl vinyl ketones with benzonitrile *N*-oxide, 3-nitrobenzonitrile *N*-oxide, and diphenylnitrylimine, the less substituted multiple bond is the more reactive [170]. Hept-2-en-5-yn-4-one (CXII) reacts with diphenylnitrylimine both via the double bond and the triple bond, forming a pyrazoline (CXIII) and a pyrazole (CXIV): [171]



(CXIII) (CXIV)

The reaction of butynone with the methyl nitrolic ester of ethyl nitroacetate (CXV) yielded 82% of the corresponding aziridine derivative. Its formation is probably associated with a rearrangement of the substituted 4-isoxazoline (CXVI) obtained in the first stage of the reaction via the general dipolar 1,3-cycloaddition mechanism [172]:

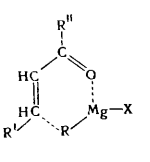


(CXV) (CXVI)

XIV. ETHYNYL KETONES IN ORGANOMAGNESIUM SYNTHESIS

The interaction of vinyl ketones with organomagnesium compounds has been investigated by many Soviet and foreign workers. In particular, special studies have been made on the effect of polar and steric factors on the ratio of the 1,2- and 1,4-addition products [172–174].

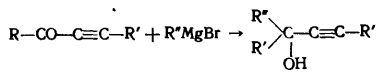
The literature data for the involvement of ethynyl ketones in organomagnesium synthesis are not quite so systematic. It has been suggested [175] that the 1,4-addition of organomagnesium reagents to vinyl ketones proceeds via an intermediate stage involving an unstable chelate complex (CXVII). In ethynyl ketones, this type of steric distribution of reacting molecules is difficult owing to the linear configuration of the –C≡C group and therefore the main reaction pathway should be 1,2-addition to the carbonyl group:



(CXVII)

Indeed, as early as 1907 Kohler [176], showed that phenyl magnesium bromide enters into the 1,2-addition reaction

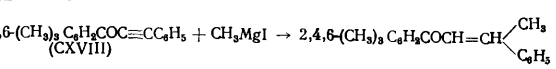
with benzoylphenylacetylene and into the 1,4-addition reaction with its vinyl analogue. Subsequently, studies of the interaction of ethynyl ketones with aromatic [177,178], aliphatic [178,179], and acetylenic [178,180,181] organomagnesium compounds and also of silylethynyl ketones with Iotsich reagents [182] showed that in most cases the main reaction products are tertiary α-ethynyl alcohols (or diethynyl alcohols):



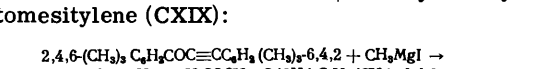
(R=R'=Alk, Ar; R"=Alk, Ar, HC≡C—)

Traces of unsaturated ketones (1,4-addition products) were detected chromatographically in some cases [178].

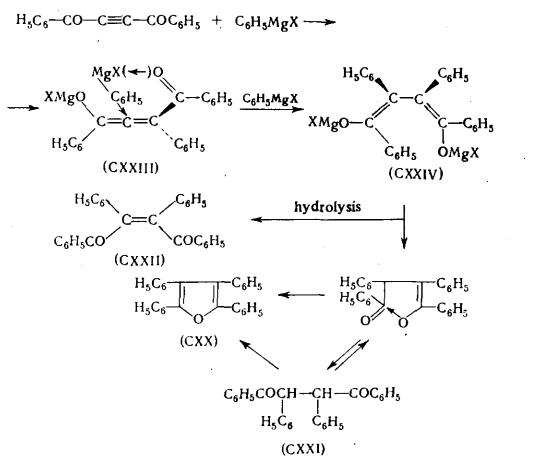
As a result of the presence of bulky substituents at the carbonyl group, the main reaction pathway becomes 1,4-addition. Thus mesitoylphenylacetylene (CXVIII), in which approach to the carbon atom of the carbonyl group is hindered, readily condenses with methylmagnesium iodide and with phenyl- and mesitylmagnesium bromides via the mechanism [183]:



The condensation of mesitoylmesitylacetylene with methylmagnesium iodide yields two isomeric products, namely the *cis*- and *trans*-isomers of β-methylmesitylideneacetomesitylene (CXIX):



Another instance of 1,4-addition occurs in reactions of dibenzoylacetylene [184] which can react, in principle, with Grignard agents via the following pathways: (1) two consecutive 1,2-additions; (2) two consecutive 1,4-additions; (3) a combination of consecutive 1,2- and 1,4-additions. In fact, the reaction with C_6H_5MgX takes place via mechanism (2), since hydrolysis of the reaction mixture yielded tetraphenylfuran (CXX), *meso*-dibenzoyldiphenylethane (CXXI), the thermodynamically unstable *cis*-dibenzoylstilbene (CXXII), and a small amount of *trans*-dibenzoylstilbene [184]. This is probably due to the high reactivity of the allenolate (CXXIII), which is an $\alpha\beta$-unsaturated ketone with a sterically accessible β-carbon atom:

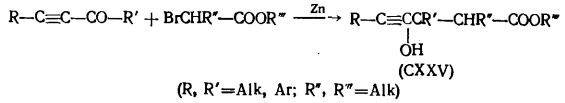


A further 1,4-addition to the allenolate (CXXIII) leads to the saturated diketodienolate (CXXIV), the subsequent hydrolysis of which yields the unsaturated diketone (CXXII), the saturated diketone (CXXI), and tetraphenylfuran (CXX). It is interesting that the main reaction product is *cis*-dibenzoylstilbene (CXXII) when hydrolysis is carried out in effective contact with air. The formation of *cis*-dibenzoylstilbene is minimal if the reaction is performed in an atmosphere of nitrogen.

The differences in the modes of addition of the Grignard reagent to dibenzoylacetylene and phenylbenzoylacetylene cannot be accounted for solely by steric factors. Indeed the electrophilic properties of the triple bond in dibenzoylacetylene are greatly enhanced under the influence of the strong inductive $-I$ effect of the two benzoyl groups. Phenylbenzoylacetylene has only one acetylenic carbon atom in the β-position relative to the carbonyl group, the electrophilic properties of which are somewhat weakened, in relation to dibenzoylacetylene, by the electron-donating influence of the phenyl group [184]:



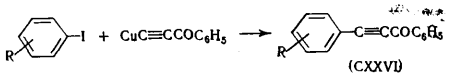
Mono- and di-substituted ethynyl ketones readily enter into the Reformatskii reaction with α-bromoacetic esters in the presence of metallic zinc, forming β-hydroxyacid esters (CXXV) in a yield of 45–62%: [185,186]



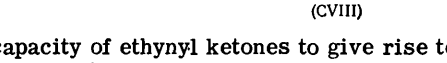
(R, R'=Alk, Ar; R", R"'=Alk)

XV. REACTIONS OF THE ETHYNYL HYDROGEN ATOM

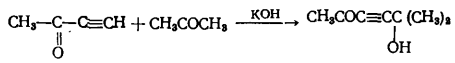
The mobility of the hydrogen atom in monosubstituted ethynyl ketones is due not only to the nature of the triple bond itself but also to the presence of the electron-accepting carbonyl group [187]. Treatment of ethynyl ketones with ammoniacal solutions of silver(I) and copper(I) salts by the usual method yielded the corresponding silver and copper acetylides, which can be used as starting materials for the synthesis of various disubstituted ethynyl ketones (CXXVI) and monosubstituted arylacetylenes [188]:



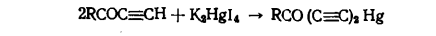
1,4-Dibenzoylbutadiyne (CVIII) has been synthesised by oxidative dihydrocondensation from benzoylacetylene [168]:



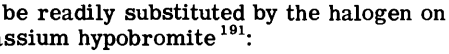
The capacity of ethynyl ketones to give rise to acetylides on treatment with powdered potassium hydroxide permits their employment for the synthesis of the simplest homologues of aliphatic α-ethynylketoalcohols (CXXVII) under the conditions of the Favorskii reaction [189]:



Mercury derivatives of ethynyl ketones can be obtained with the aid of K_2HgI_4 in alcoholic alkali [190]:



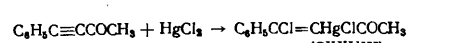
The ethynyl hydrogen atom in the ethynyl ketone molecule can be readily substituted by the halogen on interaction with potassium hypobromite [191]:



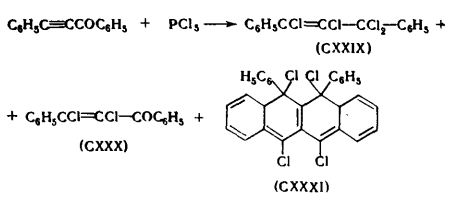
XVI. VARIOUS REACTIONS

Apart from the reactions already discussed, a number of interactions of a non-general type have been described for ethynyl ketones.

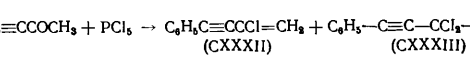
Acetylphenylacetylene readily combines with mercury(II) chloride in saturated aqueous sodium chloride solution to form a crystalline substance (CXXVIII) which is fairly stable in an acid medium but decomposes readily on heating to the initial compounds [192]:



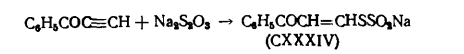
When phosphorus pentachloride is allowed to react with ethynyl ketones, there is both addition of chlorine to the multiple bond and substitution of the carbonyl oxygen by chlorine. The mode of reaction depends on the reactant ratio and on the structure of the ethynyl ketone. Thus the reaction of PCl_5 with benzoylphenylacetylene yields a mixture of products consisting of 1,2,3,3-tetrachloro-1,3-diphenylpropene (CXXIX), 2,3-dichloro-1,3-diphenylprop-1-en-3-one (CXXX), and compound (CXXXI):



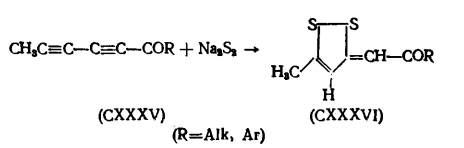
With acetylphenylacetylene, two products are formed—3-chloro-1-phenylbut-3-en-1-yne (CXXXII) and 3,3-dichloro-1-phenylbut-1-yne (CXXXIII) in proportions of 3 : 1: [193]



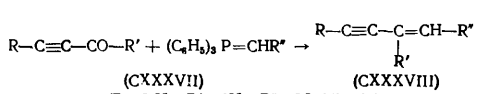
When ethynyl phenyl ketone reacts with sodium thiosulphate in a polar solvent in the presence of acid, the thiosulphate residue adds to the triple bond [194]. The reaction takes place on heating with a 69% yield of the vinyl ketone (CXXXIV):



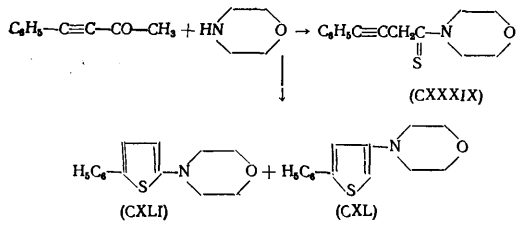
Diacetylenic ketones (CXXXV) react with sodium disulphide in methanol to form cyclic acetonylidenedithiols (CXXXVI) in quantitative yields [195]:



The interaction of ethynyl ketones with phosphorane (CXXXVII) and its derivatives leads to the corresponding ethynyl vinyl compounds (CXXXVIII): [196]

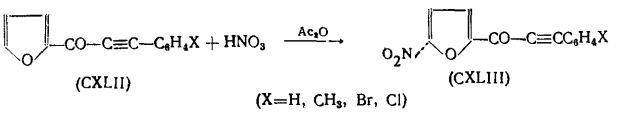


Nightingale and Carpenter [197] carried out the Willgerodt reaction with acetylphenylacetylene using morpholine and sulphur and obtained a 51% yield of a compound to which they attributed the structure of γ-phenylethynylthioacetomorpholide (CXXXIX):

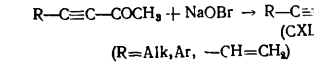


Ozonolysis of the morpholide (CXXXIX) resulted in the cleavage of the molecule to benzoic acid, but the attempt at hydrolysis to phenylacetic was unsuccessful. Later Bacchetti et al. [198] demonstrated by infrared and NMR spectroscopy that the main product of this reaction is 4-(*N*-morpholonyl)-2-phenylthiophen (CXL) with a small admixture of the isomer (CXLI). [198]

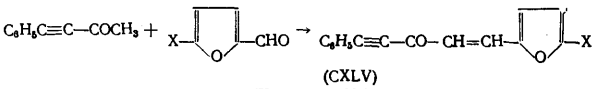
Apart from the reactions involving the multiple bond and the carbonyl group, ethynyl ketones can also enter into reactions involving substituents. For example, when furyl phenylethynyl ketones (CXLII) were nitrated in acetic anhydride, 5-nitrofuryl phenylethynyl ketones (CSLIII) were obtained. It was noted that the rate of nitration depends to a considerable degree on the benzene ring substituent conjugated with the furan ring [199]:



The haloform cleavage of ethynyl ethyl ketones takes place fairly smoothly with formation of substituted propiolic acids (CXLIV). [200] The reaction can be used as a method for the synthesis of α-ethynylcarboxylic acids:



The crotonic condensation of ethynyl methyl ketones with aldehydes in an alkaline medium has been used to synthesise symmetrical ethynyl vinyl ketones (CXLV): [201]



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Institute of Petrochemical
and Cold-chemical Synthesis,
Zhdanov State University,
Angarsk

U.D.C. 547.458.81

Biologically Active Cellulose Derivatives

A.D.Virnik

The review deals with the synthesis and applications of biologically active cellulose derivatives. The synthesis of cellulose derivatives with antimicrobial and haemostatic (arresting blood flow) properties, the possible fields of application of antimicrobial and haemostatic cellulose materials, the synthesis of graft copolymers of cellulose and biologically active proteins (enzymes and antigens), and medical applications of cellulose derivatives containing ionogenic or complex-forming groups are considered.
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I. INTRODUCTION

One of the rapidly developing fields in the chemistry of macromolecular compounds concerns the synthesis of new polymers and the chemical modification of known natural and synthetic polymers carried out to obtain biologically active substances. In particular the use of polysaccharides for such syntheses is of considerable interest. At the present time both insoluble and water-soluble biologically active polymers have been obtained on their basis. For the synthesis of water-insoluble polymers, it is often useful to employ cellulose—a readily available and cheap fibre-forming polysaccharide. The synthesis of biologically active cellulose derivatives and the preparation of biologically active cellulose materials constitutes one of the most interesting and promising aspects of the general problem of the chemical modification of cellulose [1]. The principal types of biologically active cellulose derivatives and their applications are considered below.

II. CELLULOSE DERIVATIVES WITH ANTIMICROBIAL PROPERTIES

The development of methods for the synthesis of cellulose derivatives with antimicrobial properties makes it possible to create a new type of cellulose fibre—antimicrobial fibre; as will be shown below, this can be made into articles which can be employed effectively in medicine and certain branches of industry. Studies on the synthesis of biologically active cellulose derivatives by chemical addition of bactericidal and fungicidal substances to the cellulose macromolecules have developed extensively during the last decade. This method yields fibrous materials, the antimicrobial activity of which is retained after they have been used for a long time. The methods for the determination of the antimicrobial activity of cellulose derivatives (in the form of fibrous materials) have been considered by Virnik and Mal'tseva [2].

One of the main questions arising in the development of methods for the preparation of antimicrobial cellulose fibres containing chemically combined bactericidal substances is that of which type of chemical bond between the bactericidal substance and the polymer ensures an antibacterial activity of the material. To elucidate this problem, a study was made *in vitro* of the antibacterial activity of modified cellulose fibres containing bactericidal substances of the acridine series, halogenophenols, halogens, and silver and copper ions, linked to the functional groups of the modified cellulose macromolecules in different ways [3-7]. Tables 1 and 2 present data for the antibacterial activity of cellulose derivatives with different structures.

Table 1. Effect of the structure of the cellulose derivative containing a chemically combined bactericidal substance on the antibacterial activity of the material [4-6].

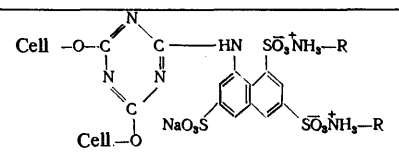
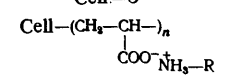
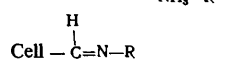
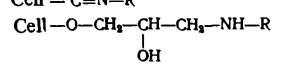
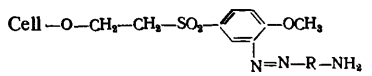
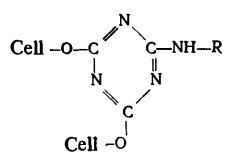
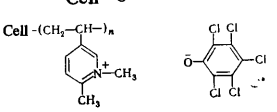
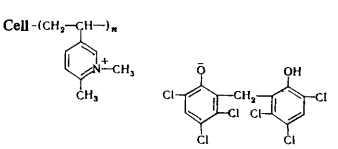
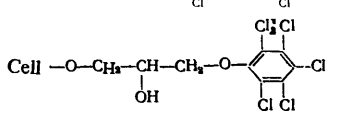
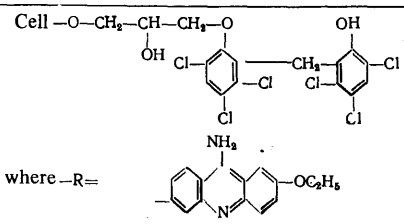
No.	Schematic structure of cellulose derivative	Antibacterial activity
1		+
2		+
3		+
4		−
5		−
6		−
7		+
8		+
9		−

Table 1. (contd.)

No.	Схе Schematic structure of cellulose derivative	Antibacterial activity
10		—

The results show that only those cellulose derivatives in which the bactericidal substance is attached to the polymer by ionic, labile covalent, or coordinate linkages possess antibacterial activity. An example of compounds of this type is provided by cellulose derivatives containing 6,9-diamino-4-ethoxyacridine (Table 1, Nos. 1 and 2) or halogenophenols (Table 1, Nos. 7 and 8). The second type includes cellulose derivatives containing 6,9-diamino-4-ethoxyacridine (Table 1, Nos. 3) or the residue of an *N*-halogenoamino-compound (Table 2, Nos. 5 and 6). Polymers of the third type include complexes of a graft copolymer of cellulose and poly-2-methyl-5-vinylpyridine (or polyvinylpyrrolidinone) with iodine (Table 2, Nos. 7 and 8). Compounds with a stable covalent bond between the cellulose derivative and the bactericidal substance do not exhibit antibacterial activity.

The antibacterial activity of cellulose derivatives in which silver ions are linked to various functional groups increases with the number of silver ions split off from the functional groups of the polymer in an aqueous medium.

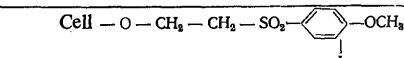
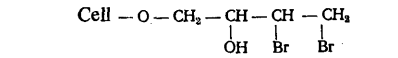
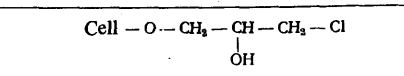
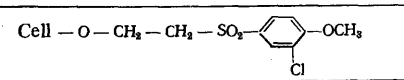
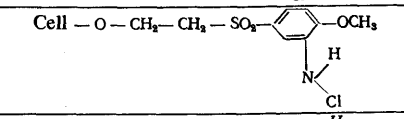
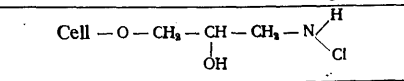
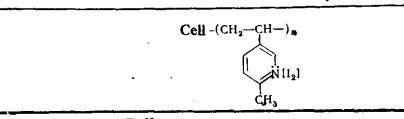
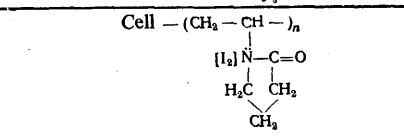
It has been shown [7] that, for the same iodine content, materials obtained from graft copolymers of cellulose and polyvinylpyrrolidinone have more pronounced antibacterial properties than materials obtained from a graft copolymer of cellulose and poly-2-methyl-5-vinylpyridine. This finding can be explained by the fact that owing to the *–I* effect of the carbonyl group in the graft polyvinylpyrrolidinone, the electron density of the nitrogen atom is lower than in the poly-2-methyl-5-vinylpyridine graft copolymer and therefore the stability of the complex formed with iodine by grafted polyvinylpyrrolidinone is also lower.

The sum total of the data quoted above lead to the conclusion that the antibacterial activity of the cellulose derivatives investigated is due to the fact that bactericidal substances interact with the microbial cell after being split off from the polymer carrier.

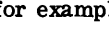
Cellulose derivatives with antimicrobial properties have been synthesised on the basis of two main principles: (1) by treating cellulose with bactericidal and fungicidal substances containing reactive functional groups capable of interacting with the hydroxy-groups of cellulose or (2) by a preliminary chemical modification of cellulose in order to introduce into its macromolecules reactive functional groups which are subsequently used to combine with bactericidal and fungicidal substances.

The bactericidal and fungicidal substances employed in the synthesis of antimicrobial cellulose derivatives have been mainly (1) metal ions, (2) quaternary ammonium bases, (3) antibiotics, (4) halogens, (5) phenol derivatives,

Table 2. Effect of the structure of the cellulose derivative containing chemically combined halogens on the antibacterial activity of the material [5].

No	Schematic structure of cellulose derivative	Antibacterial activity
1		—
2		—
3		—
4		—
5		+
6		+
7		+
8		+

(6) organometallic compounds, and (7) compounds of the nitrofuran series.

It has been suggested [8] that antimicrobial cellulose derivatives containing metal cations and quaternary ammonium bases be obtained by treating cellulose with compounds having the general formula A–B–A, where A $\overset{\oplus}{X}[BC^+]$ are groups capable of reacting with the cellulose hydroxyls (for example, N=C=O, CHO, and ), B is the residue of an aliphatic, aromatic, or heterocyclic compound, X is an ionogenic group, (for example, COO^- and SO_3^-), and $[BC^+]$ is a cation with antimicrobial properties (for example, Ag^+, Hg^{2+}, Cu^{2+}, Zn^{2+}, and R_4N^+). Salts of hydroxymethyl derivatives of levulinhydantoin, *N*-(carboxymethylaminomethyl)melamine, and sulphomethylurea [8] as well as salts of 1,3-di(hydroxymethyl)-5-sulphoethyltetrahydro-1,3,5-triazin-2-one, 5-(*m*-carboxyphenyl)-1,3-di(hydroxymethyl)tetrahydro-1,3,5-triazin-2-one, and 5-carboxymethyl-1,3-di(hydroxymethyl)tetrahydro-1,3,5-triazin-2-one [9] can be used as compounds of this kind. To synthesise derivatives with antimicrobial properties, cellulose (in the form of a fabric) is treated for a short time at 20°C with an aqueous solution of the salt of one of the above compounds containing an acid catalyst, after which the reaction is carried out at 100–150°C.

Antimicrobial derivatives of cellulose containing metal and quaternary ammonium cations and also antibiotics with basic groups have been synthesised from a graft copolymer

of cellulose and poly(acrylic acid) or poly(methacrylic acid)[10,11], a weakly substituted carboxymethyl ether of cellulose[12,13], 2-carboxy-2-chloroethyl ether of cellulose[14], cellulose sulphate[15], cellulose treated with 2,4-dichloro-6-[*N*-(3′,6′,8′-trisulpho-1′-naphthylamino)]-1,3,5-triazine[11,16,17] or dyed with active dyes containing ionogenic groups[17,18] and cellulose phosphate[19] and xanthate[20].
In most of the above studies ionogenic groups were initially introduced into the cellulose macromolecule and then used to combine with the bactericidal substance. An example is provided by the synthesis of antimicrobial cellulose derivatives on the basis of the graft copolymer of cellulose and poly(acrylic acid):

$$\text{Cell}-(CH_2-\underset{\underset{COONa}{|}}{CH}-)_n + [BC^+]\,A^- \rightarrow \text{Cell}-(CH_2-\underset{\underset{COO^-[BC^+]}{|}}{CH}-)_n + Na^+A^-,$$

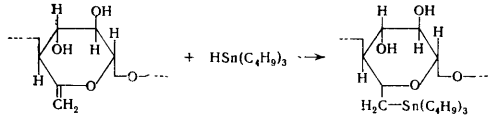
where $[BC^+] = Ag^+$, Cu^{2+}, R_4N^+, or NH_3^+ - neomycin and $A^- = NO_3^-$, SO_4^{2-}, or Cl^-. The addition of bactericidal cations to the carboxy-groups of viscose fibre has been described[21,22].

Graft copolymers of cellulose with poly-2-methyl-5-vinylpyridine, polyvinylpyrrolidonone, and other polymers containing lactam rings have been used to synthesise antimicrobial cellulose materials containing iodine[6,23,24]. Cellulose derivatives containing chemically combined antimicrobial substances belonging to the group of chlorinated phenols have been synthesised on the basis of the graft copolymer of cellulose and poly-2-methyl-5-vinylpyridine[6,11].

An organotin derivative of cellulose was synthesised for the first time by the reaction of ethynyldeoxycellulose and triphenyltin bromide according to the following scheme[25]:

$$\{C_6H_7O_2(OH)_{3-x}(C{\equiv}CNa)_x\}_n + BrSn(C_6H_5)_3 \rightarrow \{C_6H_7O_2(OH)_{3-x}[C{\equiv}C-Sn(C_6H_5)_3]_x\}_n$$

The synthesis of tin-containing deoxy-derivatives of cellulose, cellulose ethers, and graft copolymers of cellulose has now been achieved[26-28]. Tributylstannyldeoxycellulose has been synthesised by the radical addition of tributyltin hydride to 5,6-celluloseen according to the reaction



and by nucleophilic substitution via the reaction of cellulose iodotoluene-*p*-sulphonate or toluene-*p*-sulphonate with tributylstannyl-lithium[28].

When cellulose toluene-*p*-sulphonate was employed as the starting material, the reaction took place according to the mechanism

$$\{C_6H_7O_2(OH)_{3-x}(O-SO_2-C_6H_4-CH_3)_x\}_n + LiSn(C_4H_9)_3 \rightarrow$$
$$\rightarrow \{C_6H_7O_2(OH)_{3-x}[Sn(C_4H_9)_3]_x\}_n$$

Tributylstannylthiodeoxycellulose has been obtained by treating mercaptodeoxycellulose with bis(tributyltin) oxide[28].

Tin-containing cellulose ethers have been synthesised from trialkyltin oxides and hydroxides and cellulose ethers the functional groups of which contain a mobile hydrogen atom [carboxymethyl, 2-hydroxy-3-mercaptopropyl, 2-(3′-mercapto-4′-methoxyphenyl), sulphonylethyl, and propargyl derivatives] and also by the radical addition of tributyltin hydrides to allyl and propargyl ethers of cellulose[26,28]. The reaction took place according to the following mechanisms:

$$\text{Cell}-O-CH_2-COOH + HOSnR_3 \rightarrow \text{Cell}-O-CH_2-C(=O)-O-SnR_3$$

$$\text{Cell}-O-CH_2-\underset{\underset{OH}{|}}{CH}-\underset{\underset{SH}{|}}{CH_2} + HOSnR_3 \rightarrow \text{Cell}-O-CH_2-\underset{\underset{OH}{|}}{CH}-\underset{\underset{S-SnR_3}{|}}{CH_2}$$

$$\text{Cell}-O-CH_2-CH_2-SO_2-C_6H_3(SH)-OCH_3 + HOSnR_3 \rightarrow$$
$$\rightarrow \text{Cell}-O-CH_2-CH_2-SO_2-C_6H_3(S-SnR_3)-OCH_3$$

$$\text{Cell}-O-CH_2-C{\equiv}CH + HOSnR_3 \rightarrow \text{Cell}-O-CH_2-C{\equiv}C-SnR_3$$

$$\text{Cell}-O-CH_2-CH{=}CH_2 + HSnR_3 \rightarrow \text{Cell}-O-CH_2-CH_2-CH_2-SnR_3$$

$$\text{Cell}-O-CH_2-C{\equiv}CH + HSnR_3 \rightarrow \text{Cell}-O-CH_2-CH{=}CH-SnR_3$$

(R = alkyl residue)

Graft copolymers of cellulose and poly(trialkylstannyl acrylate) or poly(triarylstannyl acrylate) have been synthesised by the reactions of the graft copolymer of cellulose and poly(acrylic acid) with trimethyl-, triethyl-, and triphenyltin hydroxides and also with bis(tributyltin) oxide. The structures of some of the tin-containing cellulose derivatives synthesised were confirmed by Mössbauer spectroscopy[29]. Data on the effect of the structure and amount of the organotin compound chemically combined with cellulose on the antimicrobial properties of the polymer have been published[28,30].

The synthesis of tin-containing derivatives with the general formula cell $-O-SnR_3$ by treating cellulose (or its ether) with alkoxytrialkyltin or the potassium alkoxide derivative of cellulose with trialkyltin chloride has been described[31-33]. However, organotin compounds of the type R_3SnOR' are readily hydrolysed even by atmospheric moisture. It is noteworthy that a high antimicrobial activity of organotin and organomercury derivatives of cellulose can be achieved by introducing into the macromolecules of modified cellulose a very small amount of tin or mercury (0.1–0.2% of the weight of cellulose).

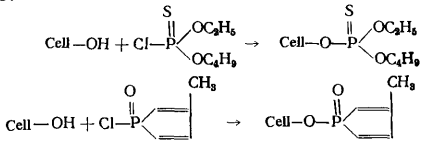
To synthesise organotin derivatives, cellulose ethers and esters containing the residues of unsaturated aliphatic, aromatic, or heterocyclic compounds [2-hydroxybut-3-enyl[34,35], allyl[36], benzyl[37], and 2-(3′-amino-4′-methoxyphenyl)sulphonylethyl[38] cellulose ethers as well as cellulose esters with methacrylic[39,40], sorbic[41,42], oleic[43,44], salicyclic[45,46], furancarboxylic[47,48], and cinnamic[44,47] acids] were mercurated (usually with mercury acetate). As an example one may quote the mercuration of cellulose methacrylate:

$$\text{Cell}-O-\underset{\underset{O}{\|}}{C}-\underset{\underset{CH_3}{|}}{C}=CH_2 \xrightarrow{Hg(OOC-CH_3)_2} \text{Cell}-O-\underset{\underset{O}{\|}}{C}-\underset{\underset{HgOOC-CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-\underset{\underset{OH}{|}}{CH_2}$$

Mercury-containing cellulose derivatives have also been synthesised by mercurating with mercury acetate cellulose dyed by active dyes[49], graft copolymers of cellulose with polyacrylonitrile and poly-2-methyl-5-vinylpyridine[50] as well as styrene and benzyl methacrylate[51]. In the preparation of antimicrobial bast fibres, there is no need for a preliminary modification of the fibres; in this case the initial bast fibres can be mercurated to impart to them antimicrobial properties[52,53], since the lignin macromolecules, which enter into the composition of such fibres, contain aromatic residues, which readily interact with mercury salts.

The synthesis of antimicrobial cellulose derivatives containing antimony from cellulose and antimony(III) acid chlorides or esters have been described [54]. The structures of the compounds synthesised may be represented schematically by the formulae Cell–O–$SbCl_2$ and Cell–$OSb(OC_2H_5)_2$. According to patent data [55–57], various phosphorus-containing cellulose derivatives have been synthesised by treating cellulose with phosphorochloridothioates, phosphorochloridothioites, phosphoroisothiocyanatidates, and phosphoroisothiocyanatidites and also with chlorophosphacyclopentenes in organic solvents.

The reactions of cellulose with *O*-n-butyl *O*-ethyl phosphorochloridothioate and 1-chloro-1-oxo-3-methylphosphacyclopentene proceed according to the following mechanisms:



Antimicrobial derivatives of cellulose containing residues of a nitrofuran bactericidal substance have been obtained by the reaction of partly hydrolysed cellulose triacetate with β-(5-nitrofuryl)acrolein [58,59]. According to the literature, esters of cellulose and unsaturated aliphatic acids [60–62] and also 2-carboxy-2-chloroethyl ether of cellulose [14] acquire antimicrobial properties on bromination or substitution with thiocyanate groups [14].

The properties and possible applications of antimicrobial cellulose fibre materials were investigated in detail in recent years. Under practical conditions, the most detailed studies have been made on the antimicrobial cellulose fibre materials containing chemically combined copper or silver ions and also hexachlorophene. It has been shown [30,63–66] that antimicrobial cellulose fibre materials containing various chemically combined bactericidal substances suppress the development of pathogenic microorganisms or postoperative infections. Experiments carried out under the conditions of the surgical clinic of the Antarctic station (Vostok) and also in undertakings of the food industry showed that, when clothing made of antimicrobial fibres containing chemically combined hexachlorophorene and silver or copper ions is used, the population of microorganisms on human skin and on the clothing itself is reduced severalfold compared with the values obtained when ordinary clothing is worn [67–69]. It has been shown [70,71] that, when surgical masks made of antimicrobial muslin containing chemically combined silver ions are worn, the frequency of infection after operative wounds by the microflora from the surgeon's nasopharynx is approximately three times smaller than under the conditions when a mask of ordinary muslin is worn. This suggests that articles made of antimicrobial fibres can be used as a means whereby the microbial population can be reduced and the risks of microbial infection in surgical clinics, in undertakings of various branches of industry, and also in prolonged expeditions can be lowered. Clothing made of antimicrobial fibres can be used not only under specific conditions when the risk of infection by microorganisms is great or the conditions of personal hygiene are difficult but also in ordinary life.

Modified cellulose materials containing chemically combined chlorophenols, organomercury and organotin compounds, or iodine are resistant to the action of mildew and suppress the development of pathogenic fungi causing fungal affections of the feet [30,72,73]. Such fibres can apparently be used to manufacture stockings, socks, and shoe insoles for use in the prophylaxis of common fungal affections.

It has been shown [74] that antimicrobial cellulose fabrics containing chemically combined copper or silver ions can be usefully employed for the packing of sterile surgical instruments. Packing made of antimicrobial fabrics ensures that the surgical instruments remain sterile for several months. The employment of such packing is particularly important for first aid posts and also in rural and mountainous localities.

At the present time antimicrobial materials containing chemically combined hexachlorophene and copper or silver ions have been recommended by the Ministry of Health of the USSR for use in medical practice and their manufacture has begun.

Antimicrobial fibres and non-woven filtering materials made from them can be usefully employed for the sterilisation of air supplied to the fermentation units in the manufacture of antibiotics and in the apparatus for the preparation of blood components [75–78]. In the filtration of air, micro-organisms are not only mechanically trapped by the filtering materials, but also destroyed by the action of the bactericidal substances in the fibres. Non-woven antimicrobial filtering materials ensure the necessary degree of purification and sterilisation of air over a period of several months and their employment increases the reliability of the operation of the filter. In contrast to the filtering materials made of the usual non-antimicrobial fibres, they do not require periodical sterilisation [76,77]. It has been shown [79] that antimicrobial cellulose fabrics containing silver ions bound to the carboxy-groups of grafted poly(acrylic acid) can be used to disinfect river water.

Antimicrobial cellulose materials will presumably prove useful also in other fields.

III. CELLULOSE DERIVATIVES WITH HAEMOSTATIC PROPERTIES

The problem of the arrest of blood flow in surgical operations, particularly of blood flow from small vessels, is important in surgery and still cannot be regarded as finally solved. The use of haemostatic preparations greatly simplifies the technique of the surgical operation and shortens its duration. Despite the positive results achieved when expensive and scarce haemostatic preparations made from donated blood are employed, the search for new haemostatic preparations, based on polysaccharides including cellulose rather than on proteins, is being continued.

Among haemostatic preparations obtained on the basis of cellulose, the so called monocarboxycellulose, synthesised at the end of the 1930's by oxidising cellulose with nitrogen oxides [80], has been investigated in greatest detail. According to the literature [81–84], during the Second World War oxidised cellulose already began to be used in surgical practice as a haemostatic preparation absorbable by the organisms.

Reviews [83,84] and other publications [85–95] have been devoted to monocarboxycellulose. On oxidation by nitrogen oxides, carboxy-groups are formed in the cellulose macromolecule mainly at the sixth carbon atom of the elementary unit. Apart from the main process involving the oxidation of primary hydroxy-groups, secondary hydroxy-groups are also oxidised, which results in the formation of keto- and then carboxy-groups with rupture of the pyran ring [89,90]. Some of the carboxy-groups react with the

hydroxyls in the same cellulose macromolecule (with formation of lactones) or with the hydroxyls of another macromolecule (with formation of esters)[88]. The products always contain a certain amount of nitrate groups. The presence in the oxidised cellulose macromolecule of elementary units containing simultaneously carboxy- and carbonyl groups is responsible for the low resistance of the oxidised cellulose macromolecule to the action of water at an elevated temperature[96]. The sterilisation of cellulose materials oxidised with nitrogen oxides by treatment in an autoclave (this sterilisation procedure is common in surgical clinics) is impossible, since treatment with steam leads to complete degradation of monocarboxycellulose. Haemostatic preparations made from monocarboxycellulose are sterilised by γ-radiation[97,98] or are prepared under sterile conditions[99].

It has been suggested[83,84,96,98] that the calcium salt of monocarboxycellulose, which is prepared by treating oxidised cellulose for a long time with an aqueous solution of calcium chloride, be employed as a haemostatic material. Experiments showed that the calcium salt is an effective haemostatic preparation. During recent years a number of patents and publications have appeared[98,100-104] in which new forms of haemostatic preparations made from oxidised cellulose or various improvements to the technological process for the manufacture of monocarboxycellulose have been proposed. The addition of various antimicrobial substances (tubazid, kanamycin, rivanol, norsulphazol, and streptomycin) to the functional groups of cellulose oxidised by nitrogen oxides and the use of the resulting compounds in surgical operations have been described[97,104-108]. According to the literature, the employment of absorbable haemostatic preparations with antimicrobial activity simplifies the technique of surgical operations and promotes the prophylaxis of post-operative complications. A prolonged action of the above medicinal substances is achieved at the same time.

Nowadays cellulose oxidised by nitrogen oxides is used in surgical practice but the wide-scale employment of this haemostatic preparation which can be absorbed by the organisms is difficult owing to the complicated apparatus required for the technological preparation of monocarboxycellulose and particularly its calcium salt and by the necessity to manufacture the haemostatic material under sterile conditions or the employment of γ-radiation for its sterilisation.

In the patent literature, it has been suggested that haemostatic preparations in the form of tablets consisting of salts of the carboxymethyl ether of cellulose[109] and also salts of cellulose sulphate and ethers of cellulose and aliphatic hydroxyacids be employed to make solutions for the impregnation of bandaging materials[110-112].

Several years ago, a new haemostatic cellulose material, non-absorbable in the organism, which consists of the calcium salt of the graft copolymer of cellulose and poly(acrylic acid), was proposed[113-117]. In contrast to the haemostatic preparations of monocarboxycellulose, this material is sterilised in an autoclave where its haemostatic properties and stability are hardly altered. The graft copolymer of cellulose and the calcium salt of poly(acrylic acid) was synthesised by three methods[113-117]: (1) by grafting poly(acrylic acid) to cellulose and subsequently treating the resulting graft copolymer with a solution of calcium hydroxide or the calcium salt of a weak acid: (2) by grafting poly(methyl acrylate) to cellulose and then hydrolysing the ester groups of the resulting copolymer with a solution of calcium hydroxide: (3) by grafting the calcium salt of poly(acrylic acid) to cellulose using calcium acrylate as the monomer.

The third method of preparation of the haemostatic material is the most rational, since, in contrast to acrylic acid and methyl acrylate, calcium acrylate is involatile, which greatly simplifies the technology of the synthesis. The synthesis of the graft copolymer of cellulose and poly(acrylic acid) using calcium acrylate as the monomer has been described in a number of studies[118-120]. Wide-scale clinical tests showed that the haemostatic material is useful in surgical practice and it has been recommended by the Ministry of Health of the USSR for use in medicine. Haemostatic muslin is now being manufactured by a continuous process[117].

IV. GRAFT COPOLYMERS OF CELLULOSE AND BIOLOGICALLY ACTIVE PROTEINS

Water-insoluble graft copolymers of cellulose and biologically active protein are of considerable theoretical and practical interest. The synthesis of graft copolymers of cellulose with enzymes and antigens has been most thoroughly investigated. These compounds are obtained by the interaction of cellulose derivatives containing various reactive groups with proteins. However, one must bear in mind that under these conditions several reactive groups of one cellulose macromolecule can interact with several functional groups of one protein macromolecule. There are at present no reliable data concerning the structures of these compounds and therefore we shall henceforth refer to them as graft copolymers.

Water-insoluble graft copolymers of cellulose and enzymes can be used as specific catalysts and can be removed from the reaction sphere at any instant. The employment of these copolymers permits the solution of many problems, which is impossible when the usual water-soluble enzymes are used, such as, for example, the isolation of pure products of the enzymatic decomposition of a substrate, the activation of the enzyme with subsequent complete removal of the activating substance, and sorption with subsequent isolation and investigation of enzyme inhibitors[121]. Water-insoluble graft copolymers of cellulose and antigens, which have been called immunosorbents, are used to sorb antibodies for their quantitative determination and isolation in a pure form with the aim of subsequent investigation of their structures and properties[122,123]. In the synthesis of water-insoluble graft copolymers containing antigens, it is more useful to employ hydrophilic polymers, particularly cellulose, and not hydrophobic synthetic polymers, for example polystyrene, since non-specific sorption of proteins on hydrophilic cellulose materials is much weaker than on hydrophobic synthetic polymers[123].

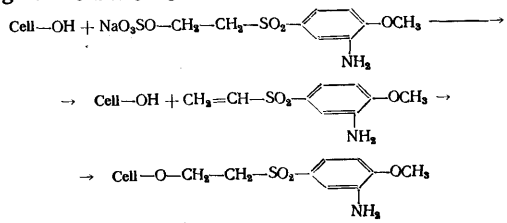
The initial cellulose derivatives employed in the synthesis of the above graft copolymers are cellulose ethers and esters containing aromatic amino-groups, the carboxymethyl ether of cellulose, the ether of cellulose and cyanuric acid chloride, the 3-chloro-2-hydroxypropyl ether of cellulose, the ester of cellulose and monobromoacetic acid, and cellulose derivatives containing epoxy-rings.

The synthesis of a graft copolymer of cellulose and a protein using as the starting material a cellulose derivative containing aromatic amino-groups was achieved for the first time at the beginning of the 1950's.[124] In this investigation the *p*-aminobenzyl ether of cellulose was diazotised and then introduced into the azo-coupling reaction with the antigen. Subsequently the ester of cellulose and

p-aminobenzoic acid and *m*-aminobenzyloxymethylcellulose were used, together with the *p*-aminobenzyl ether, for coupling with enzymes and antigens [124-137]. The cellulose derivatives used in the synthesis of graft copolymers were obtained by treating cellulose with *p*-nitrobenzoyl chloride, *p*-nitrobenzyl chloride, or *N*-(*m*-nitrobenzyloxymethyl)pyridinium chloride followed by reduction of the nitro-groups.

A simpler method for the synthesis of cellulose derivatives containing aromatic amino-groups was proposed in a study [138] where cellulose was treated in an aqueous medium in the presence of sodium carbonate with the sulphate esters of 2-amino-4-(β-hydroxyethyl)sulphonylanisole or 4-(β-hydroxyethyl)sulphonylaniline. 2-(3′-Amino-4′-methoxyphenyl)- and 2-(4′-aminophenyl)-sulphonylethyl ethers of cellulose were synthesised in this way.

The first of the above cellulose ethers was synthesised according to the scheme



The amino-derivatives of cellulose obtained were used to synthesise graft copolymers of cellulose with antigens and enzymes [139-143].

It has been shown [128,129] that the amount of antigen adding to cellulose can be increased sharply by employing a highly dispersed suspension of the cellulose ether containing aromatic amino-groups. The suspension can be obtained by the reprecipitation of the above ether from a cuprammonium solution. Later it was demonstrated [144] that this highly dispersed suspension can also be prepared by substituting the cellulose ether containing aromatic amino-groups with xanthate (in order to obtain a cellulose ether-ester soluble in alkali) with subsequent decomposition of the ester groups in the presence of sulphuric acid. The amounts of antibodies sorbed on the immunosorbents prepared in this way is 500–1000 mg per gramme of immunosorbent and the degree of non-specific sorption of the protein amounts to only 1 mg per gramme of immunosorbent [123].

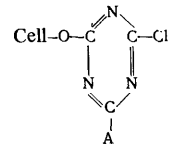
Recently it has been suggested that graft copolymers of cellulose and biologically active proteins be synthesised from 3-(4′-aminophenoxy)-2-hydroxypropyl [145,146] and *N*-[3′-(*p*-aminophenyl)butyryl]-2-aminoethyl [147,148] ethers of cellulose. However, one should note that these methods for the introduction of amino-groups into the cellulose macromolecule have no advantages over those described above.

One must also note that in immunosorbents where the protein is attached to the polymeric carrier via azo-groups a certain amount of antigen is gradually split off [149]. This is probably due to the formation during the synthesis of diazoamino-compounds, which are gradually cleaved during the storage of the immunosorbent.

The carboxymethyl ether of cellulose was synthesised for the first time for coupling with protein by Michael and Evers [150], the azide obtained from the hydrazide of the carboxymethyl ether of cellulose being introduced into the reaction. Later this method was employed to synthesise the graft copolymers of cellulose with various antigens and enzymes [130,133,151-158]. It was suggested [150-161] that the reaction between carboxymethylcellulose and protein be carried out in the presence of carbodi-imide derivatives. This method of synthesis for graft copolymers, which is simpler than the procedure involving the preparation of the azide of carboxymethylcellulose as an intermediate, has been used recently to synthesise various graft copolymers of cellulose and biologically active proteins [162-165].

The reaction between carboxymethylcellulose and protein can also be achieved in the presence of the Woodward reagent—*N*-ethyl-5-(3′-sulphophenyl)isoxazole [166].

The use of the ester of cellulose and monobromoacetic acid [167-171], the 3-chloro-2-hydroxypropyl ether of cellulose [143,149], and the ester of cellulose and cyanuric acid chloride with the general formula



where A = O–Cell, OH, NH_2, NH–CH_2COOH, etc. [143,149,172-175], as starting materials in the synthesis of graft copolymers of cellulose and biologically active proteins is of considerable interest. The synthesis of these cellulose derivatives is comparatively simple and the reaction between them and proteins can be achieved more simply than with cellulose derivatives containing aromatic amino-groups or carboxy-groups. A cellulose ether containing amino-groups has been treated [176] with an active dichlorotriazine dye (one of the chlorine atoms in the dye molecule reacted with the cellulose ether) and was then allowed to react with the protein (the second chlorine atom in the dye molecule reacted with the functional groups of the protein).

The graft copolymer of cellulose and poly(glycidyl methacrylate) [149], the 3-(4′-isothiocyanatophenoxy)propyl ether of cellulose, and the 3-allyloxy-2-hydroxypropyl ether of cellulose mercurated with mercury acetate [177] were also employed in recent years for coupling with biologically active proteins. In the last case, the mercapto-groups of the protein react with the mercury atoms attached to the alkyl residues of the cellulose ether. Cellulose has been treated [178,179] with cyanogen bromide in an alkaline medium and then a protein was coupled to the iminocarbonate groups formed. The synthesis of a graft copolymer of cellulose and a protein by treating the aminoethyl ether of cellulose and a protein with glutaraldehyde has also been described [180,181].

Likewise, the coupling of enzymes to the carboxymethyl and diethylaminoethyl ethers of cellulose and its phosphate ester via ionic linkages has been achieved [182]. When enzymes are coupled to cellulose by covalent linkages, their activity as a rule decreases. This may be due to the modification of the active centre of the enzyme, a change in the conformation of the enzyme macromolecule, and steric hindrance arising when the enzyme linked to cellulose interacts with the substrate (particularly a high-molecular-weight substrate).

It has been shown [130] that the activity of the graft copolymer of cellulose and its enzymes in relation to a polymeric substrate can be lower than in relation to low-molecular-weight model compounds. This phenomenon can probably be accounted for by steric factors. The same cause may be used to explain the finding [130] that the activity of chymocrypsin linked to carboxymethylcellulose increased with the degree of swelling of the carboxymethylcellulose and reached a maximum when a water-soluble carboxymethylcellulose was employed.

It has been shown in several studies that the addition of enzymes to cellulose not only permits the synthesis of specific catalysts which can be readily removed from the reaction sphere but also reduces the inactivation of the enzyme by external factors and its self-degradation [121,130,145,146,152,154,163]. Interesting results were obtained [137] in the immunisation of animals by the graft copolymer of cellulose and an antigen. In this case a greater amount of antibodies was formed in the animal organism than in immunisation by the soluble antigen. On repeated (after several months) immunisation of animals, to which the graft copolymer of cellulose and the antigen had been administered previously, with the soluble antigen, an extremely intense and prolonged synthesis of antibodies was observed. Their amount exceeded by a factor of 10–20 the amount of antibodies formed on repeated immunisation when the first immunisation was with the soluble antigen. Despite a number of attempts [134,161,167], hitherto it has not been possible to synthesise a graft copolymer of cellulose and an antibody capable of sorbing considerable amounts of the antigen [123].

Graft copolymers of cellulose and enzymes can be used in laboratory practice for preparative and analytical purposes (including clinical analyses), for the simulation of enzymatic processes in living organisms where the enzymes are frequently linked to cellular structures, and in industry and medicine [182]. According to the literature [182], the industrial manufacture of certain cellulose derivatives (bromoacetylcellulose, the *p*-aminobenzyl ether of cellulose, and the carboxymethyl ether of cellulose and its hydrazide), which are employed for coupling to biologically active proteins, has already begun.

As shown above, the synthesis and properties of graft copolymers of cellulose with enzymes and antigens has been investigated in greatest detail. However, bearing in mind that at the present time the advances in the chemistry of macromolecular compounds are being increasingly used for the solution of problems in biochemistry, biology, and medicine, one may expect that in the next few years it will be useful to synthesise water-insoluble graft copolymers of cellulose with other biologically active proteins and polymers incorporating polypeptide chains. The chemical fixation of the above polymers on cellulose should be achieved via functional groups which do not affect their biological activity. Therefore an increase of the number of cellulose derivatives containing various reactive groups, the development of simpler methods for synthesising graft copolymers of cellulose and proteins, and also detailed studies of the interaction of cellulose derivatives with biologically active proteins and of the effect of the structure of graft copolymers on their properties are of great interest.

V. MEDICAL APPLICATIONS OF CELLULOSE DERIVATIVES CONTAINING IONOGENIC OR COMPLEX-FORMING GROUPS

A much smaller number of studies have been made on the possibility of employing in medicine cellulose derivatives containing ionogenic or complex-forming groups. In the middle 1950's, an attempt was made to employ a plasma substitute solution of carboxymethylcellulose polymerised and substituted to different extents [183–185]. The optimum effect in experiments on animals was achieved when a 3% solution of the sodium salt of carboxymethylcellulose (degree of substitution about 0.8, degree of polymerisation 70–100) was used. However, these studies were not developed further because another polysaccharide (dextran) was found to be more useful for the preparation of a plasma substitute.

Cellulose sulphate as well as the sulphates of other polysaccharides are known to have anticoagulant properties (they prevent the clotting of blood); however, owing to its high toxicity, it has not been used for this purpose [186,187]. Cellulose phosphate can be employed as a filtering material for the extraction of calcium ions from the blood of donors for the purpose of its conservation [188–190]. In the presence of an excess of calcium in the organisms of patients, cellulose phosphate can be administered *per os* to sorb calcium ions in the intestine and to remove them from the organism [191–193].

Graft copolymers of cellulose with poly(acrylic acid) and poly-2-methyl-5-vinylpyridine (in the form of fabrics) have been used to prepare radioactive applicators for the treatment of skin diseases [194,195]. These materials are obtained by attaching to the acid and basic groups of the graft copolymers of cellulose the cations and anions of radioactive isotopes respectively. The addition of radioactive isotopic ions to the functional groups of graft cellulose copolymers ensures uniform emission from the entire surface of the radioactive applicator, which enhances its efficiency.

The antithrombogenic cellulose membranes for the dialysis of blood, obtained by coupling heparin to cellulose films with anion-exchange properties, have aroused considerable interest [196,197]. Cellulose materials with anion-exchange properties were obtained in the above investigations by treating cellulose with aziridine.

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Thus considerable advances have now been achieved in the synthesis of biologically active cellulose derivatives. Antimicrobial cellulose derivatives containing chemically combined bactericidal and fungicidal substances of different types have been synthesised. The effect of the structure of the cellulose derivatives containing chemically combined bactericidal substances on their antibacterial activity has been investigated. A study has been made of the properties and possible applications of antimicrobial cellulose fibre materials and their manufacture has begun. Methods have been developed for the synthesis of cellulose derivatives with haemostatic properties and their industrial manufacture has been achieved. Various procedures for the synthesis of the graft copolymers of cellulose and biologically active proteins (mainly enzymes and antigens) have been developed and some of the properties of such compounds have been investigated. Cellulose derivatives containing ionogenic or complex-forming groups have been used as independent biologically active compounds or as polymeric carriers for various biologically active substances.

One may expect that further development of studies in this field will yield interesting data and will make it possible to produce new biologically active polymeric materials based on cellulose.

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Linear Stoichiometry of Chemical Reactions

G.G.Filippov and M.E.Erlykina

The description of complex chemical reactions in terms of linear algebra (linear stoichiometry) is being increasingly employed in chemical and chemical engineering practice. The review deals with methods for the solution of the most frequently encountered problems in thermodynamics and kinetics involving linear combinations of stoichiometric equations.
The bibliography includes 61 references.

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I. INTRODUCTION

Stoichiometry is defined as the "branch of chemistry including the laws of quantitative relations between the reactants, the derivation of chemical formulae, and the derivation of chemical reaction equations".[1] In a wider sense, stoichiometry includes also the application of the laws of conservation of matter and energy to systems in which physical and chemical changes take place[2]. These definitions are formulated regardless of the mathematical procedures for the solution of problems of the above class.

In the present review, linear stoichiometry is understood as the description of complex chemical reactions in terms of concepts of linear algebra. The employment of a unifying procedure involving vectors and matrices permits the maximum enhancement of a characteristic feature of stoichiometry—the derivation of general results without a detailed knowledge of all the characteristics of the phenomenon being investigated.

The language and methods of linear algebra[3-5] are widely employed in applied mathematics[6] and are becoming increasingly necessary in the development of a modern theory of contact and diffusion processes in chemical engineering[7-9]. This review deals with the rules involving linear combinations of stoichiometric chemical reaction equations for which linear or power functions, such as the enthalpy of reaction or reaction rate, have been determined. Topics requiring further research in the field of matrix theory, for example systems of first-order reactions[10] and the design of kinetic experiments[11], have been deliberately omitted.

The rules involving linear combinations of stoichiometric equations were already formulated to some extent by Hess (1840). They are widely employed in chemical thermodynamics albeit without a matrix formulation[12,13]. However, when the problem involves a large number of reactions, the application of linear algebra is both useful and necessary. Moreover, the matrix formulation of the

problem constitutes to some extent the formulation of the algorithm for its solution on a computer.

An interesting set of problems arises likewise in connection with linear combination of stoichiometric equations, which should be regarded also as molecular equations, if the chemical reactions described by them from a kinetic standpoint obey the law of mass action. The study of these problems was initiated by Horiuti [14,15]. A complete and large branch of kinetics—the kinetics of steady-state reactions—has now been established [16-18]. In the theory of steady-state reactions, the methods of linear algebra find the most direct application.

II. ATOMS, MOLECULES, AND REACTIONS

Consider a closed system containing N different substances in equilibrium. The molecular formula of the ith substance consisting of a finite number of B_j atoms† can be expressed in the form

$$A_i = \sum_{j=1}^{n} \beta_{ij} B_j, \tag{1}$$

where B_j is the symbol of an atom or a charge and β_{ij} the number of atoms or charges of type B_j in a molecule A_i. Then the set of molecules A_1, A_2, ..., A_N consisting of atoms B_1, B_2, ..., B_n can be formulated as a system of equations:

$$\begin{aligned} A_1 &= \sum_{j=1}^{n} \beta_{1j} B_j, \\ A_2 &= \sum_{j=1}^{n} \beta_{2j} B_j, \\ A_N &= \sum_{j=1}^{n} \beta_{Nj} B_j \end{aligned} \tag{2}$$

or in matrix form

$$\begin{Vmatrix} A_1 \\ A_2 \\ \vdots \\ A_3 \end{Vmatrix} = \begin{Vmatrix} \beta_{11}\beta_{12} \ldots \beta_{1n} \\ \beta_{21}\beta_{22} \ldots \beta_{2n} \\ \vdots \\ \beta_{N1}\beta_{N2} \ldots \beta_{Nn} \end{Vmatrix} \begin{Vmatrix} B_1 \\ B_2 \\ \vdots \\ B_n \end{Vmatrix} \tag{3}$$

$$A = \beta B \tag{4}$$

The matrix β comprising β_{ij} coefficients with dimensions $N \times n$ is called the atomic matrix. It expresses the composition of a molecular mixture in terms of atomic components.

If one considers a reacting mixture of substances, then using the above concepts, each ith reactant A_i may be associated with a row vector in the β matrix:

$$\vec{\beta}_i = \| \beta_{i1}, \beta_{i2}, \ldots, \beta_{in} \| . \tag{5}$$

We shall suppose that the rank of the β matrix is r and therefore the number of independent $\vec{\beta}_i$ vectors is r. Suppose that these are the first r vectors (i.e. the first r rows of the β matrix). Then each succeeding vector with the indices $r+1$, $r+2$, ..., N can be expressed as a linear combination of the basis vectors

$$\beta_1, B_2, \ldots, \beta_r \tag{6}$$

$$\alpha_{r+1,r+1}\vec{\beta}_{r+1} = \alpha_{r+1,1}\vec{\beta}_1 + \ldots + \alpha_{r+1,r}\vec{\beta}_r \tag{7}$$

or

$$\alpha_{r+1,N}\vec{\beta}_N = \alpha_{N1}\vec{\beta}_1 + \ldots + \alpha_{Nr}\vec{\beta}_r$$

After transferring all the terms of these equations to one side, we obtain the following system:

$$\begin{aligned} &\sum_{i=1}^{r+1} \alpha_{r+1,i} A_i = 0, \\ &\sum_{i=1}^{r+1} \alpha_{r+2,i} A_i = 0, \\ &\vdots \\ &\sum_{i=1}^{r+1} \alpha_{Ni} A_i = 0. \end{aligned} \tag{8}$$

Eqns. (7) and (8) corresponds to chemical reaction equations.

The numbers α_{ki} are called the stoichiometric coefficients of the substance A_i in the reaction ($k = r+1, \ldots, N$; $i = 1, \ldots, r+1$). They are negative if the ith substance is the starting material in the kth reaction and positive for the products. The set of stoichiometric coefficients for the given set of reactions gives rise to the stoichiometric α matrix. In this matrix, each reaction corresponds to a row vector $\vec{\alpha}_k = \| \alpha_{k1}, \ldots, \alpha_{k,r+1} \|$.

Thus the minimum number of reactions required to describe the chemical processes in a system of N reactants is $N - r$, where N is the number of reactants A_i in the given system and r is the rank of its atomic β matrix.

The rank of the atomic matrix determines the number of independent components of the reaction mixture. This concept is used successfully in the study of equilibria. Thus for an equilibrium system in which $N - r$ reactions takes place, one can formulate a system of equations describing the chemical equilibrium conditions (the law of mass action):

$$\begin{aligned} K_1 &= f_1(\eta_1, \eta_2, \ldots, \eta_N), \\ K_2 &= f_2(\eta_1, \eta_2, \ldots, \eta_N), \\ &\vdots \\ K_{N-r} &= f_{N-r}(\eta_1, \eta_2, \ldots, \eta_N), \end{aligned} \tag{9}$$

where η_i are the numbers of models of the A_i reactants. These $N - r$ equations can be solved simultaneously with r conservation equations:

$$\sum_{i=1}^{N} \beta_{ij}\eta_i = 0 \quad (j = 1, \ldots, r) \tag{10}$$

in order to obtain the composition of the equilibrium mixture on the basis of the initial composition. It is then evident that $N - r$ relations (10) are used to determine $N - r$ values of η_i in terms of r values of independent η_i. If these r values of independent η_i are known, the composition of any equilibrium mixture is fully defined.

Key substances, the number of which is equal to the number of independent reactions, i.e. to the rank R of the stoichiometric matrix, should be distinguished from the independent components. Key substances are used as independent variables for an unambiguous description of the kinetics in systems where several reactions take place simultaneously.

The relation between the ranks of the atomic and stoichiometric matrices has been given, for example, by Aris and Mah [22]:

$$R + r \leqslant N. \tag{11}$$

Eqn. (11) is called the Gibbs stoichiometric rule.

The first application of linear algebra to stoichiometric problems involved in fact the theorems of the ranks of the

†Atoms can be understood not only as atoms in the usual sense but also various groups of atoms [19,20] and other structural fragments of the molecule, for example CH_3, $\rangle CH_2$, and $\rangle CH$ in alkanes [21].

atomic β matrix and the stoichiometric coefficient α matrix: Jouguet (1921),[23] Brinkley[24], and Pshezhetskii and Rubinshtein[25]. A convenient numerical method for finding the rank of the atomic matrix was recently described by Hanson[26]. The use of the procedures of linear algebra to give a formalised formulation of the problems arising in the study of equilibria and chemical reaction kinetics was considered by Aris[27].

Since it is frequently difficult to formulate *a priori* a system of reactants $\{A_j\}$ for the chemical reaction under investigation, the problem naturally arises of the experimental determination of the number of independent reactants and hence of the rank of the stoichiometric coefficient matrix[22]. In this case, all the N reactants in the system are determined quantitatively for the chosen initial conditions at $N + 1$ different instants $t_0, t_1, \ldots, t_N$, i.e. the composition matrix is obtained. Such analysis makes it possible to reduce the problem of the determination of the rank of the stoichiometric matrix to the determination of the rank of the composition matrix. Here the necessity to take into account the accuracy of the determination of the composition constitutes a complication.

We may note that a related problem arises also in the interpretation of the results of spectrophotometric analysis of multicomponent systems in solution[28,29].

According to Eqn. (8), any reaction can be formulated thus:

$$R_k \equiv \sum_i \alpha_{ki} A_i = 0, \tag{12}$$

where k is the number of the reaction and i the number of the substance. Here the reactions $\sum_i \alpha_{ki} A_i = 0$ and $\sum_i (\gamma \alpha_{ki}) A_i = 0$ are identical and therefore only the ratios of the stoichiometric coefficients are important. These ratios are rational numbers and for the α_{ki} it is always possible to select integral values. Different conditions which the α_{ki} must obey have been formulated[30-32] but none of these formulations has been adopted. Usually the values of α_{ki} are chosen as the smallest integral numbers compatible with Eqn. (12).

If one remembers that α is the matrix of the stoichiometric coefficients α_{ki} and the column vector of the substances $(A_1, A_2, \ldots, A_N)$ is denoted by A, Eqn. (12) can be written in the form

$$\alpha A = 0. \tag{13}$$

Since according to Eqn. (1)

$$A_i = \sum_{j=1}^{n} \beta_{ij} B_j,$$

the chemical reaction equation can be rewritten in the form

$$\sum_{i=1}^{N} \alpha_{ki} \sum_{j=1}^{n} \beta_{ij} B_j = 0. \tag{14}$$
$$(k = 1, 2, \ldots, m)$$

If the chemical reaction equation (12) is written so that the B_j are linearly independent (i.e. are in the basis of the space to which the reactants A_j belong), then, by interchanging the summation signs, we obtain

$$\sum_{j=1}^{n} \sum_{i=1}^{N} (\alpha_{ki}\beta_{ij}) B_j = 0 \tag{15}$$

and

$$\sum_{i=1}^{N} \alpha_{ki}\beta_{ij} = 0.$$
$$(j = 1, \ldots, n; \quad k = 1, \ldots, m)$$

Having designated the row vector of the elements α_{ki} by $\vec{\alpha}_k$, we obtain

$$\vec{\alpha}_k \beta = 0. \tag{16}$$

Thus for each kth reaction there is a system of n linear homogeneous equations. The coefficient $\alpha_{ki}\beta_{ij}$ must satisfy the valence rules and the laws of conservation of mass and charge.

The system of linear homogeneous equations (16) has been actually employed to find the stoichiometric coefficients α_{ki} in chemical reactions. The numbers $\alpha_{ki}\beta_{ij}$ constitute a matrix $\vec{\alpha}\vec{\beta}$ (rectangular in the general case) with dimensions $n \times N$ (the number of basis elements is smaller than the number of substances in the reacting mixture). Since the rank of this matrix is n, the system of Eqns. (16) is consistent but undetermined. A method for the solution of such systems of equations has been described, for example by Golovina[5].

It may appear strange that the set of reactions occurring in the given system is not unique but has been defined only to within the number of independent reactions. However, for many thermodynamic problems it is unimportant, since the mechanism of equilibration in the system does not affect the thermodynamic functions.

On the other hand, in the study of reaction kinetics, such an approach is unsuitable: if no account has been taken of the mechanism of equilibration, then the rate of equilibration also remains undetermined.

Nevertheless it is found that, with certain assumptions, it is possible to investigate also the problem of reaction rates if one considers stoichiometric equations which reflect the process kinetics. Such equations will be henceforth called molecular-stoichiometric. For molecular-stoichiometric equations, it is possible to define a power function of the reactant concentrations—the reaction rate. However, these equations lose the property of molecularity on being multiplied by a scalar and then added together. An interesting procedure in operations involving such equations consists in their comparison with a system of stoichiometric equations. The problems arising in this connection are considered in Section IV.

The fact that for stoichiometric and molecular-stoichiometric equations it is possible to define certain useful functions, is the reason why linear stoichiometry is of real interest for the chemist.

III. THERMODYNAMIC APPLICATIONS

It is known from thermodynamics that for any chemical reaction it is possible to determine the changes in certain functions of state (thermodynamic functions), such as the internal energy U, the enthalpy H, the Helmholtz free energy F, and the Gibbs free energy G. Since U, H, F, and G are functions of state, then for any chemical reaction under specified external conditions, for example the standard conditions (T = 298°K and p = 1 atm), one can write

$$\Delta P_k^0 = \sum_{i=1}^{n} \alpha_{ij} \Delta P_i^0, \tag{17}$$

where ΔP_k^0 is the change in any thermodynamic function (U, H, F, and G) in the chemical reaction of the number of

moles of reactants corresponding to the stoichiometric reaction equation and the ΔP_i^0 are the changes in U, H, F, and G for the formation of the individual reactants from the elements.

When the thermodynamic functions are introduced in this way, they are not always susceptible to experimental determination. Therefore one frequently employed the method of the algebraic summation of the chemical reaction equations and the corresponding thermodynamic functions. This procedure was employed for the first time by Hess to determine the enthalpies of formation of substances.

As shown in Section II, the set of reactions R_k involving a set of substances $\{A_i\}$ ($i = 1, 2, \ldots, N$) can be regarded as the vector $\vec{\alpha_k}$ in a linear vector space. Since the change in thermodynamic functions is associated with the chemical reaction, each vector $\vec{\alpha_k}$ in the space is associated with a certain number—the change in the thermodynamic function. Thus for a linear combination of vectors (reactions), these numbers obey Eqn. (17), i.e. they form linear functions in the vector space (in the space of chemical reactions) [5].

As stated in Section II, for each system of substances $\{A_i\}$ there is a minimum set $\bar{R}_k$ of reactions describing the chemical processes in the system. If for each reaction $\bar{R}_k$ forming part of the fundamental set the ΔP_k^0 are known, then for any lth linear combination of fundamental reactions,

$$R_l = \sum_{k=1}^{m} \lambda_{lk} \bar{R}_k \left(\bar{R}_k = \sum_{i=1}^{N} \bar{\alpha}_{ki} A_i \right), \qquad (18)$$

it is also possible to find ΔP_l^0 using the properties of the linear functions in the vector space [5]:

$$f(x + y) = f(x) + f(y), \qquad (19)$$

$$f(\lambda x) = \lambda f(x). \qquad (20)$$

Then, if one wants to determine the change in an unknown thermodynamic function ΔP_l^0 for a reaction Rl, one must choose a system of fundamental equations for chemical reactions with known ΔP_k^0. This system must be such that the reaction Rl is a linear combination of the $\bar{R}_k$ i.e. Eqn. (18) holds.

In practice, for example in thermochemistry, the so called thermochemical cycles are set up for this purpose. There are several methods for the determination of the coefficients λ_{lk}, one of which has been described by Luzanov [33].

Substitution of Eqn. (12) in Eqn. (18) yields

$$\sum_{i=1}^{N} \alpha_{li} A_i = \sum_{k=1}^{m} \lambda_{lk} \sum_{i=1}^{N} \bar{\alpha}_{ki} A_i. \qquad (21)$$

By changing the order of the summation and by setting the coefficients of the independent A_i equal to one another, we obtain a system of linear equations in the unknowns λ_{lk}:

$$\alpha_{li} = \sum_{k=1}^{m} \lambda_{lk} \bar{\alpha}_{ki} \quad (i = 1, \ldots, N) \qquad (22)$$

or

$$\begin{Vmatrix} \alpha_{l1} \\ \vdots \\ \alpha_{lN} \end{Vmatrix} = \bar{\alpha}^T \begin{Vmatrix} \lambda_{l1} \\ \vdots \\ \lambda_{lm} \end{Vmatrix}.$$

The number of components A_i entering into the reaction is always greater than or equal to the number of fundamental reactions. Therefore the $\bar{\alpha}$ matrix of the coefficients $\{\bar{\alpha}_{ki}\}$ will have the dimensions $m \times N (N \times m)$ for each reaction with the index l. However, the system obtained is consistent since $N - m$ equations are linearly dependent. Having chosen m independent equations and having solved the resulting system, we obtain λ_{lk}.

After the determination of λ_{lk}, the changes in thermodynamic functions in the lth reaction can be found in accordance with the properties of the linear functions (19) and (20) in terms of

$$\Delta P_l = \sum_{k=1}^{m} \lambda_{lk} \bar{P}_k, \qquad (23)$$

where $\Delta \bar{P}_k$ are the changes in thermodynamic functions for the fundametal chemical reaction equations.

Consider the following simple example from a collection of problems [34]. From a specified system of fundamental reactions for which the enthalpies of formation ΔH^0 are known,

	ΔH^0, kcal mole^{-1}
ZnS(solid) - Zn(solid) - S (orthorhom.) = 0	$\Delta H_I^0 = -44.0$
$2ZnO + 2SO_2 - 2ZnS - 3O_2 = 0$	$\Delta H_{II}^0 = -221.88$
$2SO_3 - O_2 - 3SO_2 = 0$	$\Delta H_{III}^0 = -46.88$
$ZnSO_4 - ZnO - SO_3 = 0$	$\Delta H_{IV}^0 = -55.1$

one is required to find the enthalpy ΔH_V^0 of the reaction

$$ZnSO_4 - Zn - S(\text{orthorhom.}) - 2O_2 = 0 \qquad \Delta H_V^0 = ?$$

We formulate the $\bar{\alpha}$ matrix for this system of chemical equations:

Zn	S	O_2	SO_3	SO_2	ZnO	ZnS	$ZnSO_4$
−1	−1	0	0	0	0	1	0
0	0	−3	2	0	2	−2	0
0	0	−1	−3	2	0	0	0
0	0	0	0	−1	−1	0	1

,

whereupon we have according to Eqn. (22)

$$\begin{Vmatrix} -1 \\ -1 \\ -2 \\ 0 \\ 0 \\ 0 \\ 0 \end{Vmatrix} = \begin{Vmatrix} -1 & -1 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & -3 & 2 & 0 & 2 & -2 & 0 \\ 0 & 0 & -1 & -3 & 2 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -1 & -1 & 0 & 1 \end{Vmatrix}^T \begin{Vmatrix} \lambda_1 \\ \lambda_2 \\ \lambda_3 \\ \lambda_4 \end{Vmatrix}. \qquad (24)$$

Having chosen from Eqns. (24) obtained any four which are linearly independent, we find $\lambda_1 = 1$, $\lambda_2 = 2$, $\lambda_3 = 1/2$, and $\lambda_4 = 1$ and we obtain for H_V^0

$$\Delta H_V^0 = \Delta H_I^0 + {}^1/_2 \Delta H_{II}^0 + {}^1/_2 \Delta H_{III}^0 + \Delta H_{IV}^0 =$$
$$= -(1 \times 44.0) - ({}^1/_2 \times 221.88) - ({}^1/_2 \times 46.88) - (1 \times 55.1) =$$
$$= -223.48 \text{ kcal mole}^{-1}.$$

The method of finding the thermodynamic functions for reactions from the known thermodynamic functions for fundamental reactions is suitable also for the determination of the equilibrium constants.

If the equilibrium constants for the fundamental reactions K_{Rk} are known, then since

$$\lg K_R = -\Delta F_R^0/RT, \text{ and } \lg K_{\bar{R}_k} = -\Delta F_{\bar{R}_k}^0/RT,$$

the condition

$$\Delta F_R^0 = \sum_k \lambda_k \Delta F_{\bar{R}_k}$$

leads to

$$\lg K_R = \sum_k \lambda_k \lg K_{\bar{R}_k}.$$

An example of the calculation of the equilibrium constant for the oxidation of arsenic sulphides by nitric acid from the known equilibrium constants for five fundamental reactions is quoted by Luzanov[33].

The efficiency of the method for the calculation of thermodynamic functions described above is illustrated particularly clearly in problems which give rise to large systems of equations, the solution of which requires the employment of a computer. For example, for a certain class of compounds one can consider simultaneously not one thermochemical cycle, but a set of such cycles involving a chosen set of fundamental reactions and one can find all possible linear combinations of the cycles corresponding to the formation of various compounds of the given class. A problem of this kind for boron compounds was formulated and solved by Guest and Pedley[35].

As stated above, the molecular formula of any substance can be written thus:

$$A_i = \sum_{j=1}^{n} \beta_{ij} B_j, \qquad (25)$$

where B_j are structural fragments (atoms, bonds, and groups of atoms) and β_{ij} are their numbers in the molecule. Formally, the formation of a molecule of type A_i from the structural elements can be regarded as a reaction in which the stoichiometric coefficients are β_{ij}. One can show that these "reactions" are vectors in a linear space[27].

Next, if we associate each "reaction" of this kind with a number, for example the enthalpy of formation, evaporation, and fusion or the specific volume, i.e. any extensive property $P(A_i)$ of the substance A_i, and postulate that these numbers obey the conditions

$$P(A_i + A_j) = P(A_i) + P(A_j), \qquad (26)$$

$$P(\gamma A_i) = \gamma P(A_i), \qquad (27)$$

where A_i and A_j are arbitrary substances and γ is an arbitrary real number, then P is a linear function in the given linear space. If the fundamental reaction in this space consists of the $\{B_j\}$, the linear function P can be represented by the linear formula

$$P(A_i) = \sum_{j=1}^{n} \beta_{ij} P_j, \qquad (28)$$

where β_{ij} are the coordinates of the vector A_i in the space and P_j are coefficients independent of β_{ij}.

Then, if we have a series of substances $\{A_1, A_2, \ldots, A_N\}$ for which an experimental property P is known, it is possible to formulate the following equations:

$$P(A_i) = \sum_{j=1}^{n} \beta_{ij} P_j \quad (i = 1, \ldots, N). \qquad (29)$$

These equations are inconsistent, since for real systems Eqns. (26) and (27) hold only approximately and in addition the quantities $P(A_i)$ are themselves not entirely accurate having been determined with an experimental error.

Since the rank of the "stoichiometric" matrix is in this case n, only n of the numbers $P(A_i)$ are linearly independent. The remaining $N - n$ quantities $P(A_i)$ are linear combinations of the chosen n independent $P(A_i)$. For simplicity we shall assume that the first n equations of set (29) are independent. Then any $P(A_s)$ is

$$P(A_s) = \sum_{i=1}^{n} \lambda_i \bar{P}(A_i),$$

where λ_i may be determined by solving equations of type (22). The above equation permits the determination of the unknown quantities $P(A_s)$ having chosen an appropriate system of fundamental equations with experimental $\bar{P}(A_i)$.

However, this method for the calculation of unknown physicochemical properties of substances suffers from two significant disadvantages, namely (1) the experimental errors in the quantities $\bar{P}(A_i)$ in the fundamental equations enter wholely into the required quantity $P(A_s)$; (2) this method permits the calculations of $P(A_s)$ from the given set of fundamental equations for a comparatively narrow range of compounds.

Therefore another procedure, in which the coefficients P_j in Eqn. (28) are evaluated by least squares from experimental points for a large number of compounds, is used much more frequently. Then in principle it is possible to calculate from Eqn. (28), using known values of P_j, a given property P for any compound of the given class. Methods involving this procedure have been called additive. For example, those of Souders et al.[36] and Franklin[37], Laidler[38], Bernstein[39], Allen[40], Benson and Buss[41], Tatevskii[42], and others may be included among them. The methods differ only in the way the basis (structural elements B_j) is chosen and hence have different numbers of terms in Eqn. (28). A detailed analysis of various additive methods for the calculation of the physicochemical properties of compounds and a comparison of the accuracy of the corresponding computational formulae have been carried out[43-45].

Questions relating to the mathematical formulation of the problem and the analysis of the reliability and accuracy of the results obtained by additive methods have been considered[46,47].

IV. KINETICS OF STEADY-STATE REACTIONS

A complex chemical process can be represented by a set of molecular chemical equations (the reaction mechanism) if in addition to the reactants and products one considers also "intermediates".[48,49] It is interesting that, in order to account for chemical changes in a system, it is sufficient to postulate the existence of intermediates in very small amounts. Here the situation is approximately the same as in the boundary layer theory where one introduces the hypothesis of a high property flux gradient in a very thin layer next to the wall.

Together with stoichiometry, molecular equations describe also the kinetics, i.e. they obey the law of mass action on the basis of which it is possible to determine the rate r_s for any molecular equation s included in the mechanism of the complex reaction. For ideal systems r_s is expressed as follows[8]:

$$r_s = k_s \prod_{i=1}^{N} [A_i]^{\theta_{is}} - k'_s \prod_{i=1}^{N} [A_i]^{\gamma_{is}}, \qquad (30)$$

where $\theta_{is} = |\alpha_{is}|$ for the reactants and $\theta_{is} = 0$ for the products, $\gamma_{is} = |\alpha_{is}|$ for the products and $\gamma_{is} = 0$ for the reactants, $[A_i]$ are the concentrations of the products and reactants (these can be both bulk-phase and surface concentrations), and k_s and k'_s are the concentration-independent rate constants for the forward and reverse reactions.

Suppose that the proposed reaction mechanism consists of S stages:

$$\sum_{i=1}^{N} \alpha_{is} A_i = 0 \qquad (31)$$

$$s = 1, 2, \ldots, S,$$

in which N reactants participate, including Q intermediates and $P = N - Q$ reactants and products.

By considering the rate r_i of the disappearance or evolution of the ith substance,

$$r_i = \sum_{s=1}^{S} \alpha_{is} r_s \quad (i = 1, \ldots, N), \tag{32}$$

we can obtain a system of equations describing the local rate of the chemical reaction in terms of the known rates r_s of the individual stages. However, this equation includes also the concentrations of the intermediates, which are not usually measured. The above difficulty can be obviated by adducing the classical hypothesis of the steady-state concentrations of the intermediates, according to which they should obey the following conditions:

$$\begin{gathered} r_q = \sum_{s=1}^{S} \alpha_{qs} r_s = 0, \\ q = P+1, P+2, \ldots, Q. \end{gathered} \tag{33}$$

Here α_{qs} are the stoichiometric coefficients of the intermediates q in the sth stage of the mechanism. Eqns. (33) makes it possible in many cases to express explicitly the concentrations of the intermediates in terms of those of the products and reagents and hence solve the problem. A critical analysis of the steady-state hypothesis has been carried out [50].

Horiuti [14] and also Horiuti and Nakamura [15] showed that there is another method of expressing the steady-state conditions which is more convenient for complex mechanisms than that specified by Eqns. (33). These workers suggested that one should consider linear combinations of stages involved in the mechanism of the complex reaction. The stoichiometric equations resulting from these linear combinations can be called routes. The stoichiometric coefficients of route m are of the form

$$\alpha_{im} = \sum_s \alpha_{is} \nu_{sm}, \tag{34}$$

where ν_{sm} are the so called stoichiometric numbers, i.e. multipliers for stage s, which are introduced before adding to subtracting from other stages.

Formally, we can write, as for the set of stages, an equation of type (32) for a set of routes:

$$r_i = \sum_m \alpha_{im} r_m, \tag{35}$$

where r_m is the rate for route m but the form of r_m is still unknown. By setting equal Eqns. (32) and (35) and taking into account Eqn. (34), we obtain,

$$\sum_s \alpha_{is} r_s = \sum_m \left(\sum_s \alpha_{is} \nu_{sm} \right) r_m.$$

By altering the order of summation, we find

$$\sum_s \alpha_{is} r_s = \sum_s \alpha_{is} \sum_m \nu_{sm} r_m.$$

Assuming that the coefficients of α_{is} are equal, we obtain finally

$$r_s = \sum_m \nu_{sm} r_m \tag{36}$$

Eqn. (36) describes the relation between the unknown rates for different routes and the known rates for different stages. It only remains to decide on the method of choosing the stoichiometric numbers ν_{sm}. According to Horiuti's hypothesis [14,15], the stoichiometric numbers are chosen by solving the homogeneous system of equations

$$\sum_s \alpha_{qs} \nu_{sm} = 0 \quad (q = P+1, P+2, \ldots, Q). \tag{37}$$

It is possible to show that Eqn. (37) is a consequence of the hypothesis that the concentrations of the intermediate correspond to a steady-state. Indeed Eqn. (33) can be put in the form

$$\sum_s \alpha_{qs} r_s = \sum_s \alpha_{qs} \sum_m \nu_{sm} r_m$$

and, by changing the order of summation, we find

$$\sum_m r_m \sum_s \alpha_{qs} \nu_{sm} = 0.$$

This leads to Eqn. (37). Eqn. (37) should in fact be regarded as an expression of Horiuti's steady-state condition but in the literature [17,18] this term is given to Eqn. (36).

Eqns. (37) comprise Q equations in S unknowns ν_s and $Q < S$. The number M of the linearly independent solutions of these equations is equal to the number of routes and is given by the condition $M = S - Q$. Since $Q < S$, some of the ν_s are free variables and must be fixed in order to obtain a solution to Eqn. (37).

Thus each set of molecular equations (mechanisms) can be associated with a set of stoichiometric equations (routes) and Eqns. (36) with the ν_{sm} determined from Eqn. (37) can be used to find r_m and the concentrations of the intermediates.

We shall consider as an example a complex reaction (pyrolysis of ethane) the suggested multiphase mechanism of which is of the following form [51]

$$C_2H_6 = 2CH_3^{\cdot}, \tag{I}$$

$$CH_3^{\cdot} + C_2H_6 = CH_4 + C_2H_5^{\cdot}, \tag{II}$$

$$C_2H_5^{\cdot} = C_2H_4 + H^{\cdot}, \tag{III}$$

$$H^{\cdot} + C_2H_6 = H_2 + C_2H_5^{\cdot}, \tag{IV}$$

$$2C_2H_5^{\cdot} = C_2H_4 + C_2H_6, \tag{V}$$

where C_2H_6, CH_4, C_2H_4, and H_2 are the reactants and reaction products ($i = 1, 2, 3, 4$) and $CH_3^{\cdot}$, $H^{\cdot}$, and $C_2H_5^{\cdot}$ are intermediates ($q = 5, 6, 7$).

Eqns. (37) for mechanism (I)–(V) can be formulated as follows:

$$\begin{aligned} \nu_{1m}(2) + \nu_{2m}(-1) + \nu_{3m}(0) + \nu_{4m}(0) + \nu_{5m}(0) &= 0 \quad E_1, \\ \nu_{1m}(0) + \nu_{2m}(0) + \nu_{3m}(1) + \nu_{4m}(-1) + \nu_{5m}(0) &= 0 \quad E_2, \\ \nu_{1m}(0) + \nu_{2m}(1) + \nu_{3m}(-1) + \nu_{4m}(1) + \nu_{5m}(-2) &= 0 \quad E_3, \end{aligned}$$

This system is reduced to a canomical form by the method of leading operations [52]. The essential feature of the method involves the replacement of the initial equations E_1, E_2, and E_3 by an equivalent system where a variable has a coefficient of unity in one equation and zero in all the others.

In our case the canomical system comprises the equations

$$\begin{aligned} \nu_{1m}(1) + \ldots + \nu_{4m}(0) + \nu_{5m}(-1) &= 0 \quad (E_1 + E_2 + E_3)/2, \\ \nu_{2m}(1) + \ldots + \nu_{4m}(0) + \nu_{5m}(-2) &= 0 \quad (E_3 + E_2), \\ \nu_{3m}(1) + \nu_{4m}(-1) + \nu_{5m}(0) &= 0 \quad E_2, \end{aligned}$$

and we can obtain the complete set of solutions ν_{sm} ($m = 1, 2$) of equations E_1, E_2, and E_3 by assigning any values to the independent variables ν_{4m} and ν_{5m}. We shall now consider the permissible solutions generated by trial and error:

$$\begin{aligned} m = 1: \quad & \nu_{41} = 0; \quad \nu_{51} = 1 \\ m = 2: \quad & \nu_{42} = 1; \quad \nu_{52} = 0. \end{aligned}$$

The route ν_{s1} is of the form

$$\nu_{s1}^T = (\nu_{11}, \nu_{21}, \nu_{31}, \nu_{41}, \nu_{51}) = 1, 2, 0, 0, 1).$$

Similarly

$$\nu_{52}^T = (\nu_{12}, \nu_{22}, \nu_{32}, \nu_{42}, \nu_{52}) = (0, 0, 1, 1, 0).$$

According to Eqn. (34), the stoichiometric equations for the routes are

$$2C_2H_6 = 2CH_4 + C_2H_4,$$
$$C_2H_6 = C_2H_4 + H_2.$$

We shall now find the rates for these routes on the assumption that the reactions occurring in accordance with Eqns. (I), (II), and (V) are irreversible and reactions (III) and (IV) are reversible. Equations of type (36) assume the following form in this case:

$$k_1[C_2H_6] = r_1(1) + r_2(0), \quad \text{(IA)}$$
$$k_3[\dot{CH_3}][C_2H_6] = r_1(2) + r_2(0), \quad \text{(IIA)}$$
$$k_5[\dot{C_2H_5}] - k_5[C_2H_4][\dot{H}] = r_1(0) + r_2(1), \quad \text{(IIIA)}$$
$$k_7[\dot{H}][C_2H_6] - k_8[\dot{C_2H_5}][H_2] = r_1(0) + r_2(1), \quad \text{(IVA)}$$
$$k_9[\dot{C_2H_5}]^2 = r_1(1) + r_2(0). \quad \text{(VA)}$$

We find from Eqns. (IA) and (IIA)

$$[\dot{CH_3}] = 2k_1/k_3.$$

Eqns. (IA) and (VA) yield

$$[\dot{C_2H_5}] = \sqrt{\frac{k_1}{k_9}[C_2H_6]},$$

and from Eqns. (IIIA) and (IV) we obtain

$$[\dot{H}] = \frac{\sqrt{\frac{k_1}{k_9}[C_2H_6]}(k_5 + k_8[H_2])}{k_7[C_2H_6] + k_5[C_2H_4]}.$$

Then, according to Eqns. (IA) and (IIA),

$$r_1 = k_1[C_2H_6],$$
$$r_2 = k_7[C_2H_6][\dot{C_2H_5}]\left(\frac{k_5 + k_8[H_2]}{k_7[C_2H_6] + k_5[C_2H_4]} - k_8[H_2]\right).$$

Knowing r_1 and r_2, it is easy to find the rate of consumption of ethane in the pyrolysis process from Eqn. (32):

$$r_{C_2H_6} = 2r_1 + r_2.$$

If the concentrations of the intermediates are related in some way, as sometimes happens when reactions on the surface are considered, then the above relations must be employed in addition to Eqns. (36). The results obtained, expressed by Eqn. (35), may be compared with experimental data and the adequacy of the mechanism may be tested. For reactions with several routes, a convenient method of comparing theory with experiment involves a comparison of the calculated and experimental selectivities [53, 54].

One should also note the possibility of the occurrence of reactions with several independent mechanisms. A distinctive feature of such reactions is that the number of routes involved is greater than the number of independent reactions which can occur in the given reactant system [18].

In many cases, when the intermediates are excluded, it is convenient to employ the equations proposed by Temkin [55, 56], which are related to Eqns. (36), rather than Eqns. (36) themselves. Finally, it is possible in principle to carry out numerically all the calculations based on Eqns. (36), [57] but in this case we do not have kinetic equations of type (35) in an explicit form.

Apart from facilitating the derivation of kinetic equations on the hypothesis of steady-state concentrations of intermediates, the introduction of routes provides to some extent a basis for the classification of complex reactions. Whereas previously a distinction was drawn between complex consecutive or parallel reactions, when the routes are employed, the difference between them is insignificant and such reactions are simply processes with several routes. An interesting class of complex reactions comprises processes with a single route. These include, for example, the synthesis of ammonia and methanol, the reaction of hydrogen and bromine, etc. A reaction with a single route permits a more detailed theoretical study than reactions with several routes [16, 17]. In particular, the rate of a single-route reaction can be expressed, along the route, as the difference between the rates in the forward (r'_m) and reverse (r''_m) directions and for reversible routes it is possible to find the relation between the equilibrium constant r'_m/r''_m for the route and the rate constants k_s and k'_s for the stages by introducing the so called average stoichiometric number [58, 59], which can be determined experimentally [59-61].

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The Use of Proton Magnetic Resonance in the Study of Complexones

N.A.Kostromina

The available literature data for the protonation of complexones and the formation of their complexes with diamagnetic and paramagnetic ions are reviewed. A systematic and general account is given of studies on the equilibria and kinetics of complex formation and of the structures of the complexes. Typical PMR spectra of complexones and their metal complexes are presented; quantitative characteristics obtained from PMR data (chemical shifts, spin-spin coupling constants, stability constants, and reaction rate constants) are tabulated.
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I. INTRODUCTION

Complexones are now finding extensive application in various branches of the national economy in view of the high stability and solubility of the majority of complexonates and the characteristic features of the structures of complexones responsible for their selective properties in relation to different metals. Therefore the study of metal complexes of complexones is urgently required in connection with the synthesis of new complexones with specified properties [1].

List of Abbreviations

Methylglycine	MGl
Dihydroxyethylglycine	DGl
Iminodiacetate	IMDA
Methyliminodiacetate	MIMDA
Hydroxyethyliminodiacetate	HIMDA
β-Aminoethyliminodiacetate	AEIDA
Nitrilotriacetate	NTA
NN'-ethylenediglycine	EDDA
1,2-dimethyl-*NN'*-ethylenediglycine	DMeEDDA
1,2-diethyl-*NN'*-ethylenediglycine	DEtEDDA
N-(carboxymethyl)-*NN'*-ethylenediglycine	ED3A
N-(carboxymethyl)-*N'*-(2-hydroxyethyl)-*NN'*-ethylenediglycine	HEDTA
(Ethylenedinitrilo)tetra-acetate	EDTA
(Methylethylenedinitrilo)tetra-acetate	PDTA
[(1,2-dimethylethylene)dinitrilo]tetra-acetate	BDTA
[Oxybis(ethylenenitrilo)]tetra-acetate	EEDTA
[Ethylenebis(oxyethylenenitrilo)]tetra-acetate	EGTA
(1,2-cyclohexylenedinitrilo)tetra-acetate	CDTA
[(Carboxymethyl)iminobis(ethylenenitrilo)]-tetra-acetate	DTPA
Tetramethylsilane	tms
Sodium 3-(trimethylsilyl)propanesulphonate	tms*
Nuclear magnetic resonance	NMR
Proton magnetic resonance	PMR

Infrared spectroscopy has yielded much information about the structures of the protonated forms of complexones and also their metal complexes in the crystalline state but has been much less useful in the study of the structures of complexones in solution. However, owing to the complexity of the spectra and in many cases the ambiguity of the band assignments, the data obtained have to be checked by another method.

The method which yields the most complete information about the structures of compounds in solution is that of nuclear magnetic resonance. Many proton magnetic resonance studies have been made on the protonation of complexones and the structures of complexonates in solution. The present review deals with data obtained by this method for the structures of the complexes and the equilibria and kinetics of complex formation and protonation processes.

Since the research technique is based on a comparison of the spectra of the complexones in bound and free states, in the first section of the review we shall consider the PMR spectra of complexones and data on the structures of the protonated forms of the complexones and on the microequilibria in solution as a function of pH.

II. PMR STUDY OF THE STRUCTURES OF COMPLEXONES

Complexones is the name given to compounds containing a nitrogen atom linked to oxygen-containing groups† which can readily split off and combine with protons. In all complexones there are two types of protons: (1) the labile protons of the functional groups which exchange rapidly with the protons of water and other functional groups; (2) non-labile protons forming part of the CH_2, CH, or CH_3 groups of the complexones.

†In this review only complexones containing methylcarboxyls will be considered since NMR data for other types of complexones are not available.

If the study is performed in aqueous solutions, the resonance signals of protons of the first type merge with the signal of the water protons owing to rapid exchange. In this case, the changes in the PMR spectra on protonation are investigated on the basis of the resonance of the non-labile protons[2]. The number of resonance signals in the spectrum depends on the number of non-equivalent protons in the complexone. The positions of the signals depend on the groups with which the CH, CH_2, and CH_3 groups are linked.

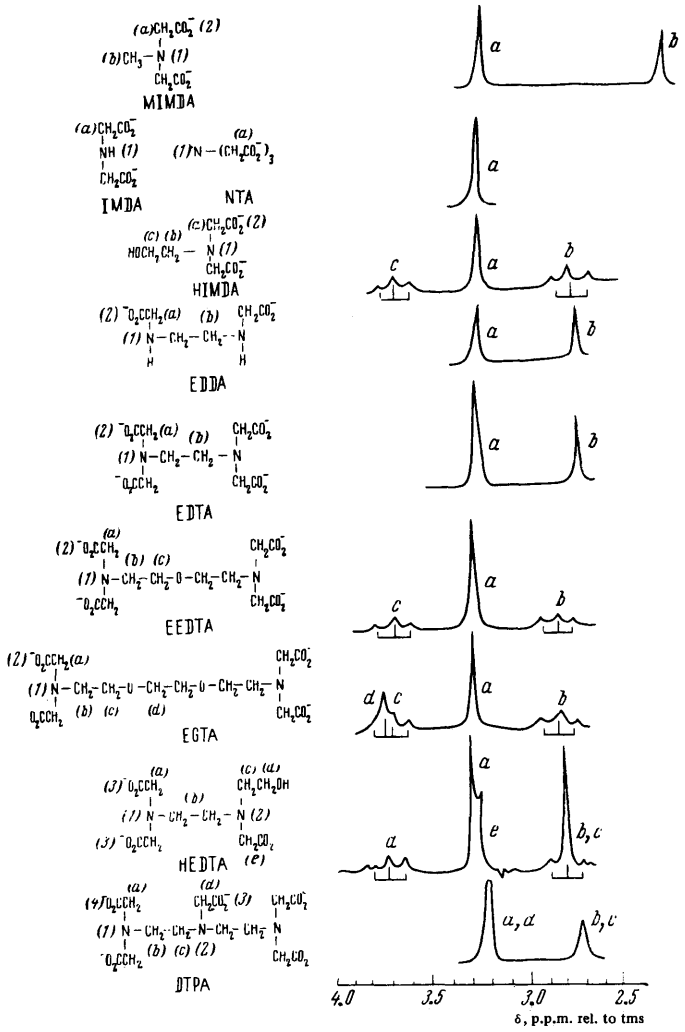


Figure 1. Characteristic proton magnetic resonance spectra of the complexones.

The changes in the position of the CH_2 signal following the addition of electron-donating groups (NR_2, COOH, OH), their protonation, and dissociation have been investigated in detail[2]. The formulae and the designations employed for the complexones investigated, the designations of the non-labile protons (*a*, *b*, *c*, *d*, *e*, ..., *l*) and of the electron-donating groups (1, 2, 3, 4, ..., *L*), and also the PMR spectra of the anions (potassium or tetramethylammonium salts) are presented in Fig. 1. The ratios of the areas and approximate calculations of the signal positions on the basis of the substitution constants carried out by Sudmeier and Reilley[2] were used to assign the signals in the spectra.

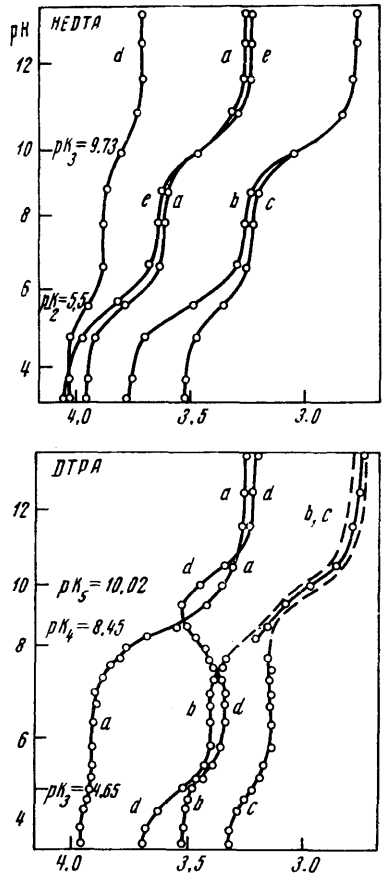


Figure 2. Shifts of the HEDTA and DTPA proton signals as a function of the pH.

If an acid is added to anions with several functional groups capable of combining with protons, microequilibria are established in solution, which include all possible combinations of the protonated and non-protonated forms. Thus, following the addition of one equivalent of acid, each functional group of the complexone may be protonated to a specified degree. This entails the descreening of the methylene protons in the immediate vicinity of the functional group protonated and a shift of their signal to a low field (Fig. 2). The magnitude of the shift depends on the nature of the electron-donating atom, its electronegativity, its position relative to the CH_2 group, and the time during which the proton remains at the electron-donating atom, i.e. on the degree of protonation of each group[2].

In the pH range where signals shifts are observed, there is a mixture of protonated and dissociated forms. The absence of signal splitting shows that rapid proton exchange takes place between these forms.

The position of the signal is defined by the equation

$$\delta_{av.} = N_A\delta_A + N_B\delta_B, \quad (1)$$

where N_A, N_B, δ_A, and δ_B are respectively the mole fractions (N) and the chemical shifts (δ) of the protonated (A) and non-protonated (B) forms. At the point of inflection where $\delta_{av} = (\delta_A + \delta_B)/2$, the concentrations of the protonated and non-protonated forms are equal.

It follows from the dissociation equation

$$\left(K = \frac{N_B[H^+]}{N_A}\right) \quad (2)$$

that, when $N_A = N_B$, the dissociation constant is equal to the hydrogen ion concentration. The dissociation constants determined from the pH–δ relation agree with the literature values [3].

Table 1. Degree of protonation of the electron-donating groups of complexones [2,5].

f_j	MGI^{-}	$IMDA^{2-}$	$MIMDA^{2-}$	NTA^{3-}
	$n=1$	$n=1$	$n=1$	$n=1$
f_1	75±6	93±3	91±5	82±2
f_2	20±5	7±3	6±3	18±2

f_j	$EDTA^{4-}$		$EEDTA^{4-}$	$EGTA^{4-}$		$HEDTA^{3-}$		$DTPA^{5-}$	
	$n=1$	$n=2$	$n=2$	$n=2$	$n=1$	$n=2$	$n=3$	$n=2$	$n=3$
f_1	53±5	96±2	96±11	96±6	42±7	87±6	26±1	85±5	80±11
f_2	−2±3	2±1	2±5	3±3	52±6	97±5	41±1	15±6	64±13
f_3	—	—	—	—	3±18	0±15	7±2	0±16	76±23

Since the addition of a proton causes the greatest shift of the signal of the CH_2 groups linked directly to the electron-donating atoms, the sequence of the protonation of these groups may be established on the basis of the pH–δ relation. The simultaneous shift of the *a* and *b* signals in the spectra of complexones derived from mono- and di-amines following the addition of the first proton to the anion (Fig. 2) shows that the nitrogen atoms are the first to be protonated, in agreement with infrared spectroscopic studies [1]. The study of the spectra of DTPA makes it possible to determine the sequence of the addition of protons to the nitrogen atoms: the middle nitrogen atom is the first to be protonated and is followed by the two extreme atoms, with proton transfer from the middle atom to the extreme atoms and the reprotonation of the middle atom [4].

The PMR method also makes it possible to obtain quantitative data for the degree of protonation of each electron-donating group [2,5]. The calculated degrees of protonation of the electron-donating groups of the complexones are listed in Table 1.

Following the addition of the number of equivalents of acid equal to the number of nitrogen atoms in the complexone, the nitrogen atoms are protonated preferentially in all the complexones investigated. However, partial protonation of the COO^{-} groups is also observed. In the presence of two nitrogen atoms, there is rapid proton exchange between them (HEDTA, EDTA, EGTA, and EEDTA). If there are three nitrogen atoms (DTPA), there is a slow exchange between the middle and extreme nitrogen atoms and rapid exchange between the extreme atoms.

CDTA, a complexone the structure of which is very close to that of EDTA and is distinguished by the presence of the cyclohexane ring, has somewhat unusual properties.

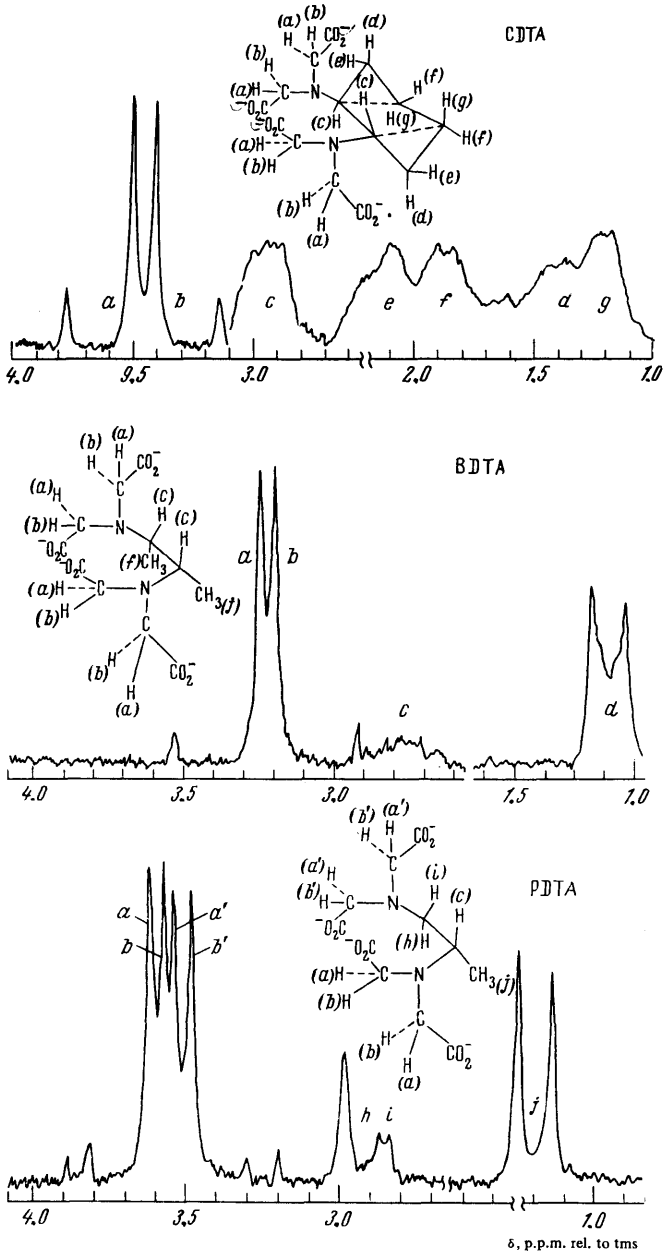


Figure 3. Characteristic spectra of CDTA, BDTA, and PDTA.

The formula of CDTA, the designations of the protons, and the spectrum of the anion are given in Fig. 3. The AB quartet [7], observed in low fields, is due to the protons of

the methylcarboxyls. The two protons in each methylcarboxyl are non-equivalent and give rise to the AB quartet, since the iminodiacetate group is linked to an asymmetric carbon atom [7]‡. The addition of the first two protons causes a shift of the quartet (the *a* and *b* signals) and of the methylidyne proton signals (*c*), the shift of the *c* signals being greater than that of the *a* and *b* signals. Consequently, here too the nitrogen atoms are the first to be protonated. There is further splitting of the *a* and *b* signals after the addition of the first proton, which has been accounted for by the formation of the bridge structure ≥N–H–N<, possibly involving the acetate groups [8].

This difference from EDTA is due to the characteristics of the disposition of the iminodiacetate groups in CDTA. The half-widths of the methylidyne proton signals, which are determined by the spin–spin coupling constant and depend on the positions of the interacting protons, demonstrated that the iminodiacetate groups in CDTA occupy the diequatorial positions. For this disposition, the distance between the nitrogen atoms is 2.2 Å, which favours the formation of a bridge structure. The presence of a linkage with two nitrogen atoms in the monoprotonated form can explain why the reaction becomes much more endothermic following the removal of this proton, in relation to the analogous reaction of EDTA. [6]

III. PMR STUDY OF THE FORMATION OF METAL COMPLEXES OF COMPLEXONES

When complexes are formed, the PMR spectra of the complexones undergo changes which can involve both a shift and a splitting of the bands. To characterise quantitatively the changes occurring in the spectra on formation of complexes with diamagnetic ions, four main parameters are employed: (1) the area of the signal; (2) the chemical shift; (3) the line half-width; (4) the spin–spin coupling constant. For paramagnetic complexes, the main parameters are the relaxation time and the contact and pseudocontact shifts.

Since the methods of investigation and the data obtained for diamagnetic and paramagnetic complexes are significantly different they will be discussed separately.

1. Diamagnetic Complexes

The study of the PMR spectra for the non-labile complexone protons led to the isolation of three groups of complexes: (1) complexes in which the M–N and M–O bonds are labile; (2) complexes in which the M–N bonds are inert and the M–O are labile; (3) complexes in which the M–N and M–O bonds are inert [9]. In the first case, the spectrum of the complex has the same form as that of the free ligand (Fig. 1). Such complexes are formed by the majority of doubly charged metals [except platinum(II) and palladium(II)] with monoamines and EDTA, [10,19] by aluminium and lanthanum with EDTA, [11,17,18] by calcium and lanthanum with HEDTA, [20,21] and by alkali metals with HEDTA. [22]

The signal shifts and the study of the δ –pH relation yielded information in such cases concerning the occurrence of complex formation in the system, and the compositions, stabilities, and structures of the complexes.

‡An analogous splitting into one or two AB quartets is observed in the spectra of other complexones containing an asymmetric carbon atom (Fig. 3).

As an example, Fig. 4 presents δ–pH relations for EDTA complexes with alkali (M : EDTA = 4 : 1) and alkaline earth (M : EDTA = 1 : 1) metals. The δ–pH curve for the potassium salt coincides with the corresponding curve for the tetramethylammonium salt, which implies that potassium does not form a complex with EDTA. The δ–pH relations for sodium, lithium, calcium, strontium, and barium indicate the occurrence of complex formation at pH > 4.

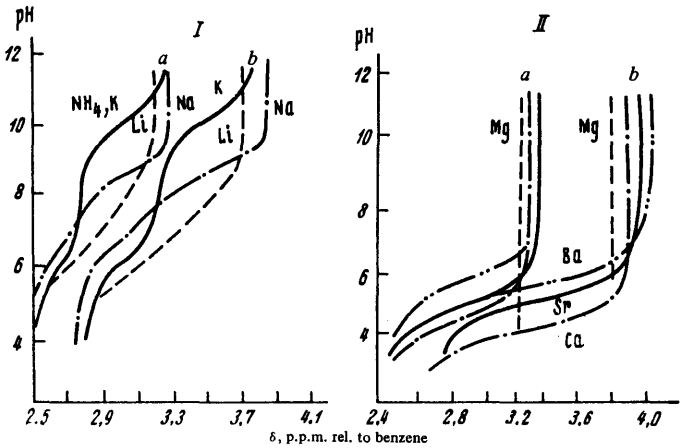


Figure 4. δ–pH relations for the EDTA complexes of alkali (I) and alkaline earth metals (II).

The presence of two rising sections in the curves for the sodium and lithium salts indicates the formation of monoprotonated complexes (in the neutral region). The shift of the signals to low fields in the acid region is due to the decomposition of the complexes. The pH values corresponding to the breakdown of the complexes characterise their stability. The stability constants of the lithium, calcium, strontium, and barium complexes have been calculated [11] from Eqn. (1) in which the subscripts A and B refer to the bound and free ligands. Similar calculations of the constants have been performed for the lanthanum and lutetium complexes of MGl, [14] MIMDA, [12] and DGl [15] and for the cadmium, zinc, and lead complexes of NTA. [16] The calculated stability constants are compared in Table 2 with the values obtained by other methods.

The low stability constants of the lithium, calcium, strontium, and barium complexes of EDTA obtained by the PMR method can be explained by the fact that in the calculation no account was taken of the formation of protonated complexes in the acid region [11].

The formation of a protonated complex in which the proton adds to the carboxy-group (only the *a* signals shift) was observed in a study of the PMR spectra of the lanthanum complex of EDTA at pH < 3. [17] The formation of mixed hydroxo-complexes of zinc and EDTA was established in the alkaline region [25]. The sharp shift of the *d* signal of HEDTA in the lanthanum complex to high fields at the solution pH corresponding to the p*K* for the hydrolysis of the 1 : 1 complex show that in this case a complex is formed in the alkaline region where the hydrogen atom dissociates from the alcoholic group of HEDTA. [21]

The study of the δ–pH relation for stable complexes (the magnesium, calcium, strontium, barium, mercury, aluminium, lead, zinc, and lanthanum complexes of $EDTA^{4-}$, the calcium and lanthanum complexes of HEDTA, and the magnesium, calcium, strontium, and barium complexes with EGTA) yielded information about the regions corresponding to the existence of the complexes: in the pH range where only one complex is present, the positions of the signals remain constant [10,11,17,19,21]. The chemical shifts in the spectra of the 1 : 1 complexes are listed in Table 3, which shows that complex formation entails signal shifts to both low and high fields. The latter are observed for complexes of alkali and alkaline earth metals with large ionic radii [26]. The signal shifts of the CH_2 protons linked to OH groups in DGl and HIMDA indicate the presence of linkages between the metal and the OH group.

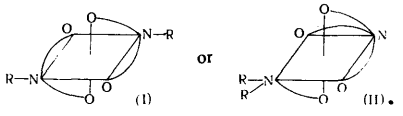
Table 2. Stability constants ($\lg K_1$ and $\lg K_2$) of metal complexes of complexones.

Formula	PMR (Ref.11)	E.m.f.* (Ref.3)	Formula	PMR (Refs. 12, 14 and 15)	pH* (Refs.23 and 24)	Formula	PMR (Ref.16)	pH* (Ref.3)
$Li_2(EDTA)^{2-}$	2.5	2.79	La (HMGl)$^{3+}$	0.6	—	Cd (NTA)$^-$	9.4	9.8
Ca (EDTA)$^{2-}$	9.4	10.6	Lu (HMGl)$^{3+}$	0.9	—	Cd (NTA)$_2^{4-}$	4.9	5.7
Ca_2 (EDTA)	—1	—	—	—	—	—	—	—
Sr (EDTA)$^{2-}$	7.6	8.6	La (MIMDA)$^+$	5.7	5.7	Zn (NTA)$^-$	10.0	10.4
Sr_2 (EDTA)	1		Lu (MIMDA)$^+$	7.07	7.1	Zn (NTA)$_2^{4-}$	3.5	—
Ba (EDTA)$^{2-}$	6.2	7.8	La (DGl)$^{2+}$	4.8	4.39	Pb (NTA)$^-$	11.4	11.39
LaH (EDTA)$_2^{4-}$	1.3	—	Lu (DGl)$^{2+}$	5.2	5.01	Pb (NTA)$_2^{4-}$	2.0	—

*Literature data adjusted to $I = 1$.

The study of the PMR spectra of alkaline earth metal, cadmium, zinc, lead, mercury, aluminium, and lanthanum complexes with different component ratios other than 1 : 1 showed that in the presence of an excess of the metal (2 : 1) calcium and strontium form compounds in which there are two metal ions for each EDTA residue, each being linked to one iminodiacetate group [27]. In the presence of an excess of the ligand (1 : 2, 1 : 3, and 1 : 5 component ratios), the formation of cadmium, zinc, lead, and lanthanum complexes containing two NTA residues per metal atom [13,16] and of a lanthanum complex with two EDTA residues [28] was established. The stability constants of the complexes were calculated (Table 2).

Complexes of metals having coordination numbers not exceeding six (lead, zinc, and cadmium), with two NTA residues can have two structures:



(I) (II).

To elucidate these structures, use was made of the spin–spin interaction between the ligand protons and the magnetic nuclei of cadmium and lead. In the 1 : 1 complexes, such interaction is observed and is reflected by a broadening of the lines in the spectra. In the complexes with two ligand species, the spin–spin interaction is not observed, i.e. the rate of dissociation increases. This can be accounted for by the decrease of the number of binding sites employed on passing from the 1 : 1 to the 1 : 2 complex, i.e. by the formation of structure(I).

The lanthanum complex with two EDTA residues was shown to have an asymmetric structure in which the second EDTA residue adds to one iminodiacetate group, the form of EDTA involved being that which predominates in solution (the protonated residue at pH 6–9 and the quadruply charged ion at pH > 9). [28] For the remaining metals investigated, only 1 : 1 complexes with EDTA have been detected [11].

Table 3. Chemical shifts of the complexone protons in metal complexes*.

Compound	δ_a	δ_b	Refs.	Compound	δ_a	δ_b	δ_c	Refs.
K_4 (EDTA)	3.14	2.61	26	K_3 (MIMDA)	2.94	2.09	—	19
Na_4 (EDTA)	3.03	2.55	11	Mg (MIMDA)	3.09	2.28	—	19
Li_4 (EDTA)	3.20	2.64	11	Ca (MIMDA)	3.06	2.15	—	19
Cs_4 (EDTA)	3.33	2.82	11	Sr (MIMDA)	2.84	1.99	—	19
Mg (EDTA)$^{2-}$	3.20	2.67	26	Ba (MIMDA)	2.86	1.99	—	19
Ca (EDTA)$^{2-}$	3.13	2.55	26	La (MIMDA)$^+$	3.14	2.18	—	12
Sr (EDTA)$^{2-}$	3.11	2.49	26	Lu (MIMDA)$^+$	3.18	2.25	—	12
Ba (EDTA)$^{2-}$	3.09	2.44	26	K_2 (HIMDA)	3.09	2.60	3.45	19
Hg (EDTA)$^{2-}$	3.34	2.85	26	Mg (HIMDA)	3.25	2.82	3.56	19
Al (EDTA)$^-$	3.56	3.14	11	Ca (HIMDA)	3.05	2.49	3.53	19
Pb (EDTA)$^{2-}$	3.55	3.15	11	Sr (HIMDA)	3.06	2.47	3.53	19
Zn (EDTA)$^{2-}$	3.36	2.85	26	La (HIMDA)$^+$	3.34	2.85	3.67	15
La (EDTA)$^-$	3.40	2.69	17	Lu (HIMDA)$^+$	3.32	2.70	3.70	15
K_4EGTA	3.30	2.65	19	K (DGl)	3.15	2.65	3.65	15
Mg (EGTA)$^{2-}$	3.43	2.75	19	La (DGl)$^{2+}$	3.35	2.70	3.86	15
Ca (EGTA)$^{2-}$	3.35	2.68	19	Lu (DGl)$^{2+}$	3.35	2.75	3.88	15
Sr (EGTA)$^{2-}$	3.24	2.55	19	H (MGl)	3.51	2.67	—	14
Ba (EGTA)$^{2-}$	3.22	2.49	19	La (HMGl)$^{3+}$	3.60	2.65	—	14
				Lu (HMGl)$^{3+}$	3.55	2.55	—	14

In this and all subsequent Tables, the chemical shifts for the diamagnetic complexes are given in p.p.m. relative to tms and the designations of the protons in DGl and MGl are the same as for HIMDA and MIMDA (Fig. 1).

In systems containing two polydentate ligands (EDTA and IMDA or NTA) and lanthanide ions, the formation of mixed complexes incorporating EDTA and IMDA or NTA residues was established [29–31]. In the mixed lanthanum complexes, the chemical shifts of the *a* and *b* signals of EDTA remain the same as in the spectrum of the 1 : 1 complex, i.e. the initial complex does not change and the second ligand species entering the complex displaces a water molecule from the inner sphere. In the spectra of the analogous lutetium complexes, the *b* signals of EDTA are displaced to high fields, which can be accounted for by a weakening of the M–N bonds with increase of the coordination number in these complexes compared with the initial $Lu(EDTA)^-$.

In the lutetium complex $Lu(EDTA)(NTA)^{4-}$, there is a slow exchange between the bound and free NTA, while in the $La(EDTA)(NTA)^{4-}$ and $Ln(EDTA)(IMDA)^{3-}$ complexes the exchange is rapid. The formation constants of the mixed complexes were calculated from the relative signal areas in the first case and from the signal shifts in the second (Table 4). For comparison, Table 4 includes the corresponding constants of the neodymium, europium, and erbium complexes evaluated by a spectrographic method [32–34].

The PMR spectra of complexes of Group I metals in the presence of an excess of ligand can be divided into three groups characterised by the rate of exchange between the bound and free ligand. 1. Rapid exchange: the number of signals does not change, the signals are

broadened, and their positions depend on the pH of the solution and are defined by Eqn. (1)—EDTA complexes of barium, strontium, and aluminium at pH < 6 and calcium and mercury in the highly alkaline region, NTA complexes of cadmium, zinc, lead, and lanthanum and IMDA and MIMDA complexes of lanthanum, yttrium, and lutetium. 2. Slow exchange: two sets of broadened signals, one of which refers to the bound and the other to the free ligand—EDTA complexes of magnesium and lead at pH < 11 and calcium, mercury, aluminium, and lanthanum at pH < 9.5, 9, 6.5, and 7 respectively. 3. Intermediate exchange: two sets of broadened signals close to one another with partial overlapping.

Table 4. Stability constants of mixed lanthanide complexes[31] ($I = 1.0$, $t = 25°C$).

Complex	lg$K$*	lg β	Complex	lg K	lg β
La(EDTA)(IMDA)$^{3-}$**	2.5±0.05	16.6	LaY(NTA)$^{4-}$	2.2±0.1	16.3
NdY(IMDA)$^{3-}$	3.8±0.1	19.2	NdY(NTA)$^{4-}$	4.8±0.1	20.2
EuY(IMDA)$^{3-}$	5.0±0.1	21.3	EuY(NTA)$^{4-}$	5.1±0.1	21.6
ErY(IMDA)$^{3-}$	3.4±0.1	20.7	LuY(NTA)$^{4-}$	2.3±0.1	20.4
LuY(IMDA)$^{3-}$	2.2±0.2	20.3			

*K and β are the successive and overall constants respectively.
**Y = EDTA.

In each of these cases the lifetime of the coordinated ligand (τ) can be represented by the following equations.

For rapid exchange:

$$\tau = \frac{\omega_{Y,MY} - N_Y\omega'_Y - N_{MY}\omega'_{MY}}{4\pi^2 N_Y^2 N_{MY}\Delta\nu_0^2}, \quad (3)$$

where ω and ω' are respectively the observed line width and the line width in the absence of exchange, N is the mole fraction, $\Delta\nu_0$ the difference between the positions of the signals due to the free and bound ligand species in the absence of exchange, and MY and Y represent the complex and the free ligand.

For slow and intermediate exchange:

$$1/\tau_{MY} = \pi(\omega_{MY} - \omega'_{MY}), \quad (4)$$

$$1/\tau_{MY} = \pi\sqrt{{}^1/_2(\Delta\nu_0^2 - \Delta\nu^2)}, \quad (5)$$

where $\Delta\nu$ is the difference between the positions of the signals due to the free and bound ligand in the test specimen.

The kinetics of ligand exchange in the systems comprising calcium and strontium with EDTA, calcium with HEDTA, and zinc, lead, and cadmium with NTA have been investigated over a wide pH range[16,20,35]. In systems comprising calcium and strontium with EDTA, the following processes were considered:

$$MY^{2-} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} M^{2+} + Y^{4-}, \quad (6)$$

$$MY^{2-} + \overset{*}{Y}{}^{4-} \underset{}{\overset{k_2}{\rightleftarrows}} \overset{*}{MY}{}^{2-} + Y^{4-}, \quad (7)$$

$$MY^{2+} + H\overset{*}{Y}{}^{3-} \underset{}{\overset{k_3}{\rightleftarrows}} \overset{*}{MY}{}^{2-} + HY^{3-}, \quad (8)$$

$$H^+ + MY^{2-} \underset{k_{-4}}{\overset{k_4}{\rightleftarrows}} M^{2+} + HY^{3-}, \quad (9)$$

$$HMY^- + H\overset{*}{Y}{}^{3-} \underset{}{\overset{k_5}{\rightleftarrows}} H\overset{*}{MY} + HY^{3-}, \quad (10)$$

$$H^+ + MY^{2-} \underset{k_{-3}}{\overset{k_3}{\rightleftarrows}} HMY^-, \quad (11)$$

$$HMY^- \underset{k_{-7}}{\overset{k_7}{\rightleftarrows}} HY^{3-} + M^{2+}. \quad (12)$$

The rate of exchange may be represented by the equation

$$-\frac{d[MY^{2-}]/dt}{[MY^{2-}]} = 1/\tau_{MY} = k_1 + k_2[Y^{4-}] + k_3[HY^{3-}] + k_5[HY^{3-}]\frac{[HMY^-]}{[MY^{2-}]} + k_7\frac{[HMY^-]}{[MY^{2-}]}. \quad (13)$$

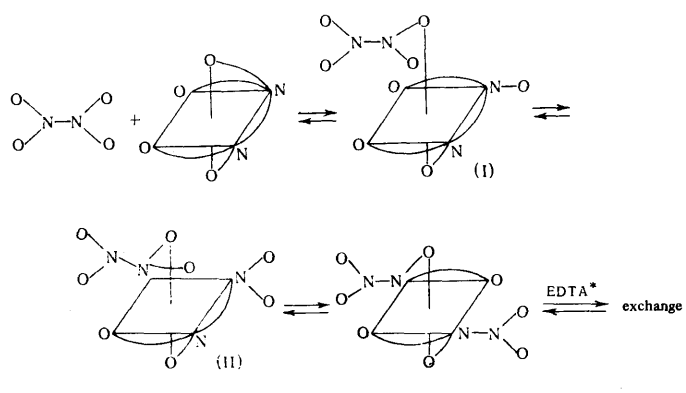
The determination of the quantities $1/\tau_{MY}$ as a function of ligand concentration at different pH permitted the calculations of the rate constants k for the reactions. The results are presented in Table 5, which also includes the rate constants for the analogous exchange reactions of the Ca(HEDTA)$^-$ system. The dissociation rate constant for Sr(EDTA)$^{2-}$ is higher than for Ca(EDTA)$^{2-}$, which agrees with the thermodynamic stabilities of the complexes[3]. The association rate constants are consistent with those for the complexes of the corresponding metals with other ligands[37], which confirms Eigen's mechanism[36].

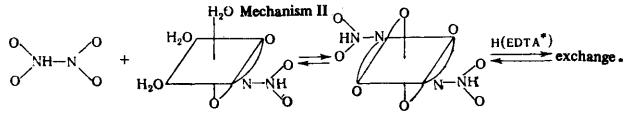
Table 5. Rate constants for exchange in metal complexes of complexones[16,20].

k_n	Ca(EDTA)$^{2-}$	Sr(EDTA)$^{2-}$	Ca(HEDTA)$^-$	k_n	Cd(NTA)$^-$	Zn(NTA)$^-$
k_1, s^{-1}	1	$3\cdot10^1$	$3\cdot10^1$	k_1, s^{-1}	<1	<1
k_{-1}, mole^{-1} s^{-1}	$2.5\cdot10^9$	$8.1\cdot10^8$	$1.3\cdot10^8$	k_2, mole^{-1} s^{-1}	$2.9\cdot10^5$	$1.8\cdot10^5$
k_2, mole^{-1} s^{-1}	$1.2\cdot10^2$	$1.1\cdot10^3$	$1.1\cdot10^3$	k_{-2}, mole^{-1} s^{-1}	$2.1\cdot10^5$	$5.1\cdot10^5$
k_3, mole^{-1} s^{-1}	5	$1.6\cdot10^2$	$2.3\cdot10^2$	k_3, mole^{-1} s^{-1}	$2.9\cdot10^2$	$5.3\cdot10^2$
k_4, mole^{-1} s^{-1}	$2\cdot10^7$	$1\cdot10^8$	—	k_4, mole^{-1} s^{-1}	$1.8\cdot10^7$	$2.0\cdot10^6$
k_5, mole^{-1} s^{-1}	$2\cdot10^5$	$1\cdot10^5$	—	k_5, mole^{-1} s^{-1}	$1.3\cdot10^7$	$6.0\cdot10^8$
k_7, mole^{-1} s^{-1}	$1\cdot10^7$	$5\cdot10^5$	—	k_6, s^{-1}	$2.2\cdot10^2$	$6.3\cdot10^2$
k_{-1}, s^{-1}	$5\cdot10^4$	$2\cdot10^4$	—	k_7, mole^{-1} s^{-1}	$1.4\cdot10^2$	—
				k_8, mole^{-1} s^{-1}	$1.2\cdot10^3$	—

The exchange reaction between the bound and free ligand species in the calcium and strontium complexes can take place either in one stage without the formation of an intermediate or in many stages with formation of an intermediate where both ligand species are linked simultaneously to the metal ion[38]. Mechanisms have been proposed for the exchange reactions (10) and (11), with formation of intermediates as the rate-limiting stage, on the basis of the available data[20,35].

Mechanism I





In mechanism(II), it is postulated that the EDTA residue in the protonated calcium and strontium complexes is linked via one iminodiacetate group. In this case, the exchange rate constants for the protonated EDTA complexes should be the same as for the complexes of the corresponding metals and IMDA. Such agreement has been observed for the strontium complexes[20].

A study has been made[16] of the kinetics and mechanism of the formation of NTA complexes of cadmium and zinc. The exchange rate constants have been determined for the following reactions:

$$M(NTA)^- \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} M^{2+} + NTA^{3-}, \quad (14)$$

$$H^+ + M(NTA)^- \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} M^{2+} + HNTA^{2-}, \quad (15)$$

$$H^+ + Cd(NTA)_2^{4-} \underset{k_3}{\overset{k_3}{\rightleftarrows}} Cd(NTA)^- + HNTA^{2-}, \quad (16)$$

$$Cd(NTA)_2^{4-} \underset{k_4}{\overset{k_4}{\rightleftarrows}} Cd(NTA)^- + NTA^{3-}, \quad (17)$$

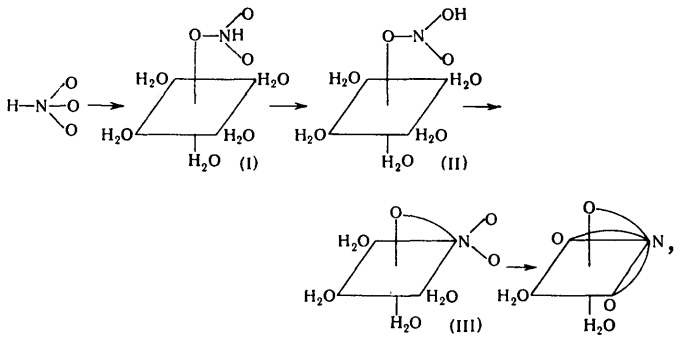
$$N\overset{*}{T}A^{3-} + Cd(NTA)_2^{4-} \underset{k_5}{\overset{k_5}{\rightleftarrows}} Cd(NTA)\,N\overset{*}{T}A^{4-} + NTA^{3-}, \quad (18)$$

$$HN\overset{*}{T}A^{2-} + Cd(NTA)_2^{4-} \underset{k_7}{\overset{k_7}{\rightleftarrows}} Cd(NTA)\,N\overset{*}{T}A + HNTA^{2-}, \quad (19)$$

$$N\overset{*}{T}A^{3-} + Zn(NTA)^- \underset{k_8}{\overset{k_8}{\rightleftarrows}} Zn(N\overset{*}{T}A)^- + NTA^{3-}. \quad (20)$$

The results are compiled in Table 5.

The data obtained demonstrated that in the exchange reaction of Cd^{2+} and Zn^{2+} with H(NTA) the rate-limiting stage is not dissociation of the water in the aquo-ion and that the rate of reaction determines proton transfer from the nitrogen atom to the carboxy-group, which can proceed either via exchange with water molecules or directly from N to O.[39] A mechanism was proposed for the formation of the complexes:



in which the rate-limiting stage is the formation of the intermediate (II).

Lutetium complexes of NTA,[13] molybdenum(V) and molybdenum(VI) complexes of IMDA, MIMDA, and NTA[40-42], cadmium[19], molybdenum[40,43,44], zirconium, hafnium[45], yttrium, and lutetium[17] complexes of EDTA, yttrium and lutetium complexes of HEDTA[21], lanthanum complexes of DTPA[46], and the majority of BDTA and CDTA[26] complexes may be included among compounds with labile M–O and non-labile M–N bonds.

If the nitrogen atom of the complexone is linked to different substituents (IMDA, MIMDA, EDTA, HEDTA, and DTPA), the formation of a non-labile M–N bond makes the two protons of the acetate group non-equivalent (H_A and H_B). The situation remains unchanged on rotation: there are three rotational configurations (Fig. 5) in each of which the H_A and H_B protons have different environments, which lead to the splitting of the signals of the protons of this group into an AB quartet[47]. Owing to the rotation of the $>N-CH_2-CH_2-N<$ group in diamine derivatives, the signals of the ethylene protons are averaged out and a singlet is produced.

A typical spectrum of the protons of the CH_2COO^- group in the EDTA, HEDTA, IMDTA, and DTPA complexes in the presence of inert M–N and labile M–O bonds is presented in Fig. 5. The PMR spectra of such complexes show new features: the spin–spin coupling constant J and the difference between the chemical shifts ($\delta_A - \delta_B$) of the non-equivalent H_A and H_B protons.

A second distinctive feature of the complexes with non-labile M–N and labile M–O bonds is slow interchelate exchange: exchange between the bound and free ligand species or ligand species in complexes with different compositions or structures. This characteristic permits the determination of the number and composition of the complexes formed in metal–ligand systems as a function of the conditions governing complex formation and can yield information about the structures of these complexes.

In the study of the spectra of the molybdenum(VI) complexes of IMDA and MIMDA[41-43], the simultaneous formation of different 1 : 1 complexes (monomers, dimers) in solution was established, the compositions of the complexes corresponding to non-stoichiometric component ratios was determined (from the signal areas), and in some cases the constants were determined and complex formation equilibrium diagrams were plotted (Fig. 6).

Data were obtained for the structures of the complexes. In the MoO_4^{2-}–$IMDA^{2-}$ system, the spin–spin interaction between the CH_2 protons and the NH proton was employed for this purpose. The spin–spin coupling constants (J_{AX} = 7.3 Hz and J_{BX} = 1.0 Hz) show that the H_A protons interact with the NH protons to a greater extent than the H_B protons. A theoretical calculation showed that the

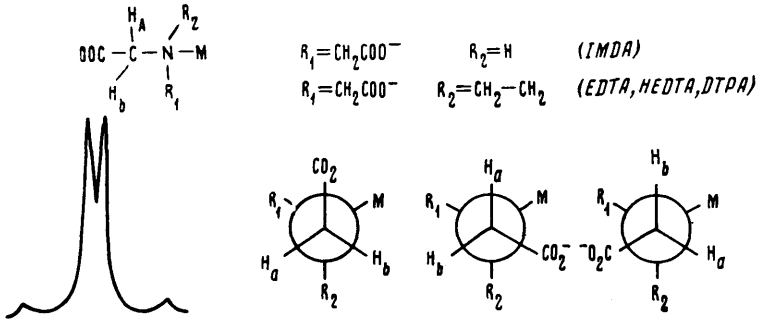


Figure 5. Characteristic spectrum of the CH_2 protons in the presence of non-labile M–N bonds.

7.3 Hz constant corresponds to an angle $\theta AX = 12°$ and the 1.0 Hz constant corresponds to an angle $\theta BX = 110°$.[41,48]

The molybdenum(VI) complexes of MIMDA give rise to a complicated spectrum with spin–spin interaction between the protons of one acetate branch and those of the other. Calculation of the spectra on the hypothesis of such interaction by a standard method[49] agreed with the experimental data[42].

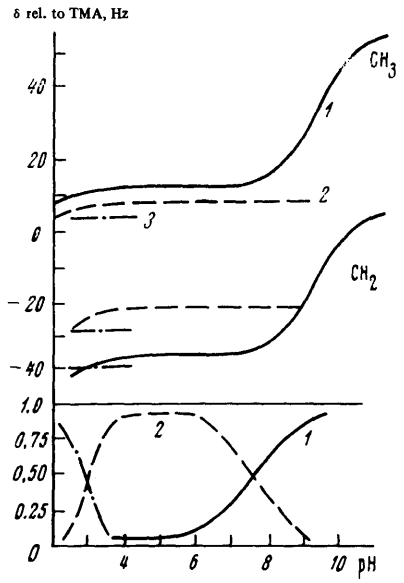


Figure 6. Complex formation equilibrium diagram for the molybdenum–MIMDA system according to PMR data: 1) free complexone; 2) monomeric complex; 3) dimer.

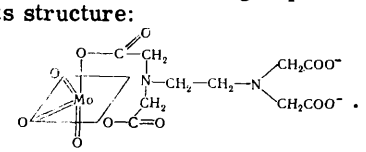
Differences were discovered between the molybdenum complexes of MIMDA and IMDA: (1) the chemical shift difference between the H_A and H_B protons in the IMDA complex is 0.65 p.p.m. in contrast to 0.27 p.p.m. for the MIMDA complex and 0.17–0.30 p.p.m. which is characteristic of all the complexes investigated with NR_3 groups. This can be explained by the fact that the substitution of a proton at the nitrogen atom by an alkyl group reduces the differences between the magnetic environments of H_A and H_B. (2) In molybdenum complexes of IMDA, the rate of exchange is higher [at a high pH the resonance signals of different specimens are averaged out ($k = 1.6 \times 10^2$ mole^{-1} s^{-1})] than for the MIMDA complexes. The reasons for this may be a decrease of steric hindrance, which facilitates attack by the free ligand.

In EDTA complexes with non-labile M–N and labile M–O bonds, the ratio of the signal areas of the bound and free ligands established that in the presence of an excess of the ligand all the metals investigated, except yttrium, form only 1 : 1 complexes. In the yttrium–EDTA system with 1 : 2 and 1 : 5 reactant ratios, a 1 : 2 complex is formed in which the second EDTA residue adds via one iminodiacetate group. This entails an increase of the mobility of the M–N bonds: the AB quartet disappears and the ethylene proton signal (*b*) shifts to a higher field[28].

In the lutetium–EDTA, zirconium–EDTA, and hafnium–EDTA systems, only 1 : 1 complexes were detected. The position of the signal of the LuY complex remains unchanged over a wide pH range (from 3 to 12), but above pH 11 a mixed hydroxo-complex is formed. This results in an increase of the mobility of the Lu–N bonds (the AB quartet disappears and the *a* and *b* signals shift to higher fields)[28]. The zirconium and hafnium complexes of EDTA give rise to spectra with signals in different positions depending on the pH of the solution, which corresponds to the two types of complexes formed: one at pH $\leq$ 3.5 (I) and the other at pH $>$ 6 (II). In the intermediate region between pH 3.5 and 6, there is a gradual transition from form (I) to form (II). Comparison with potentiometric titration data[50] established that in the region of pH $\sim$3, a simple chelate is formed and at pH 3.5 an OH group adds to the complex with possible polymerisation.

The complex formation equilibria in the molybdenum(VI)–EDTA system have been investigated as a function of the pH of the solution for Mo : EDTA $\geq$ 1.[40,44] Several complexes are formed in the system, the relative proportions of which and of the free EDTA are variable. The number of complexes in the solution was determined from the number of signals and their variation with the pH of the solution: a 1 : 1 complex, a complex with the ratio Mo : EDTA = 2 : 1, and a polymeric complex in the acid region was detected. A diagram illustrating the distribution of molybdenum among the complexes was plotted on the basis of the relative signal areas as a function of the solution pH and the stability constants of the complexes were determined ($\lg K_{MoO_3Y} = 10.7 \pm 0.3$, $\lg K_{(MoO_3)_2Y} = 19.5 \pm 0.3$).

The presence in the spectrum of the 1 : 1 complex of the signals due to two free acetate groups made it possible to establish its structure:



The complexes are protonated at pH $<$ 8 with formation of MoO_3HY^{3-}. In the complex with two MoO_3 groups, each is linked to an iminodiacetate group.

The molybdenum(V) complexes of MIMDA, NTA, and EDTA were also investigated. The paramagnetic molybdenum(V) ion forms diamagnetic complexes, which can be explained either by the formation of dimers with a linear coordination Mo–O–Mo or by the formation of dioxo-bridge complexes[43].

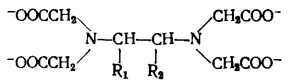
The study of the yttrium and lutetium complexes of HEDTA revealed two types of complexes with non-labile M–N and labile M–O bonds: complexes with a triply charged HEDTA residue in the pH range between 2 and 6–7 and with a quadruply charged HEDTA residue at pH $>$ 7. As for lanthanum, the formation of a complex in which the hydrogen atom in the alcoholic group has dissociated was indicated by the shift of the signal of the CH_2 group linked to the hydroxyl towards higher fields[21] and in all cases the pH at the point of inflection on the curve corresponded to the p*K* for the formation of the hydroxo-complex[51].

In the lanthanum complex of DTPA, the presence of non-labile equivalent linkages with three nitrogen atoms (C_3 symmetry) and labile linkages with the methylcarboxyls (one signal due to the ethylene proton) was established[46].

The spectroscopic parameters of certain complexes with non-labile M–N and labile M–O bonds are presented

in Table 6, which shows that in all cases where the M–O bonds in the complexes are labile the constant J is close to 17 Hz, which corresponds to unstrained bonds.

Hexadentate ligands with the general formula



(CDTA, PDTA, BDTA; Fig. 3) are very similar to EDTA.

Table 6. Spectroscopic parameters of metal complexes with non-labile M–N and labile M–O bonds.

Compound	δ_a^*	δ_b^*	J	$\sigma_A - \delta_B$	References
$(Mo^V\text{—NTA})_n^{**}$	4.35	—	—	—	43
$Lu(NTA)_2^{3-}$	3.38	—	—	—	13
$MoO_3(IMDA)^{2-}$	3.73	—	17.3	0.65	44
$MoO_3(MIMDA)^{2-}$	3.55	3.05	16.5	0.27	42
$Cd(EDTA)^{2-}$	3.41	2.64	17.1	0.17	45
$Y(EDTA)^-$	3.38	2.76	16.8	0.19	17
$Lu(EDTA)^-$	3.41	2.81	17.0	0.30	17
Zr (EDTA)	3.84	3.22	17.1	0.26	45
Hf (EDTA)	3.83	3.18	17.1	0.20	45
$MoO_2(EDTA)^{2-}$	3.57	3.73	16.7	0.31	45
$(MoO_2)_2(EDTA)^{4-}$	3.43	2.64	17.6	0.30	45
$La(DTPA)^{2-}$	3.47	2.92	17	0.20	46

*If the signals are split, the centre of the multiplet is given (δ in p.p.m. and J in Hz).
**The composition of the complex has not been established.

All these ligands differ from EDTA by the fact that the introduction of substituents into the ethylene chains hinders interconversion which in turn should be reflected in an inhibition of the M–O exchange. This is shown particularly markedly in the presence of the rigid cyclohexane ring (CDTA). Moreover, the presence of the CH_3 groups in PDTA and BDTA can lead to the appearance of isomeric forms of the complexes differing in the positions of these groups. The spectra of the complexes of BDTA with various metals are presented in Fig. 7.[26]

In the spectra of the majority of the bivalent metal complexes§, signals of two types of acetate groups are observed—two AB quartets and a doublet due to the methyl group, which is consistent with the presence of non-labile M–N and labile M–O bonds. Isomeric forms of the complexes were not observed.

Owing to the stereochemical requirements of the ring in CDTA, the methylidyne protons can have only one configuration. The inversion of nitrogen atoms is impossible and therefore the acetate groups are not involved in exchange. If two of these groups are located in one plane and the other two are in a plane at right angles to it, there should be two types of acetate groups regardless of the lifetime of the M–O bond. To obtain information about bond mobility, one can employ the constant J_{AB}: labile bonds are unstrained and J_{AB} is close to 17 Hz. However, unstrained bonds can arise also for long lifetimes. Therefore one employs also an additional method based on the broadening of the lines due to the labile bonds following the addition of a paramagnetic ion[26]. It has been established that Ag^+, all bivalent metals, and lanthanum[26,52] form complexes in which the M–N bonds are inert and the M–O bonds are labile (Fig. 8): $J_{AB} \simeq 17$ Hz.

§Exceptions are the barium and strontium complexes in which the M–N bonds are labile and the cobalt complexes in which the M–N and M–O bonds are non-labile.

The degeneration of the AB quartet to a singlet is observed for strontium, barium, zinc, hafnium(II), and lanthanum, which implies that the difference between the chemical shifts is < 0.1 p.p.m. The spectroscopic parameters of a number of metal complexes of BDTA and CDTA are presented in Table 7.

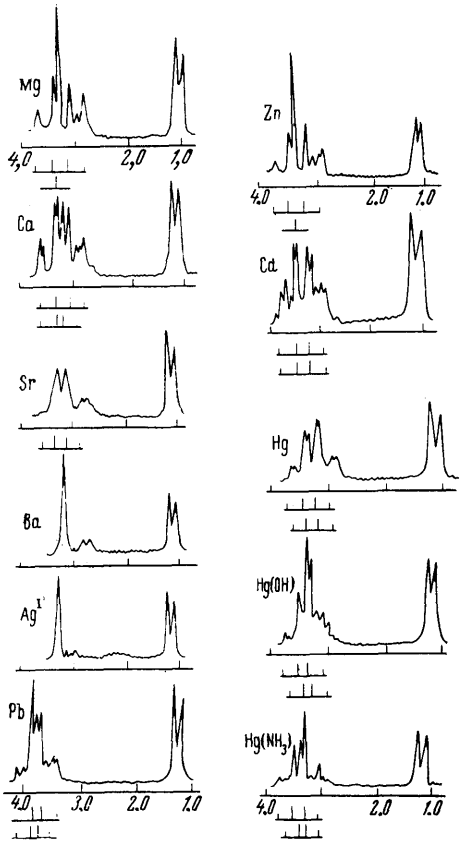


Figure 7. Characteristic spectra of metal complexes of BDTA.

In the third group of complexes (M–N and M–O bonds are inert), there is an additional splitting of the proton signals due to the non-equivalence of the groups and the inhibition of exchange and inversion. The number of AB quartets due to acetate protons varies from one (if all the acetate groups are equivalent) to two, three, or four (if all the acetate groups are non-equivalent). AB or A_2B_2 splitting is also observed.

This group includes the majority of cobalt(III), rhodium(III), platinum(II), and palladium(II) complexes. In all the complexes of the third group, there is a slow exchange between the bound and free ligand species and also between the ligand species bound in different complexes. Therefore when the solution contains two complexes or a complex and a free ligand, the spectrum becomes much more complex. Such spectra yield valuable information about the structure of the complexes, the number of binding sites in the ligand employed, the disposition of the electron-donating

group, the occurrence of *cis–trans* isomerism, and also about the equilibria and kinetics of the exchange between isomeric forms.

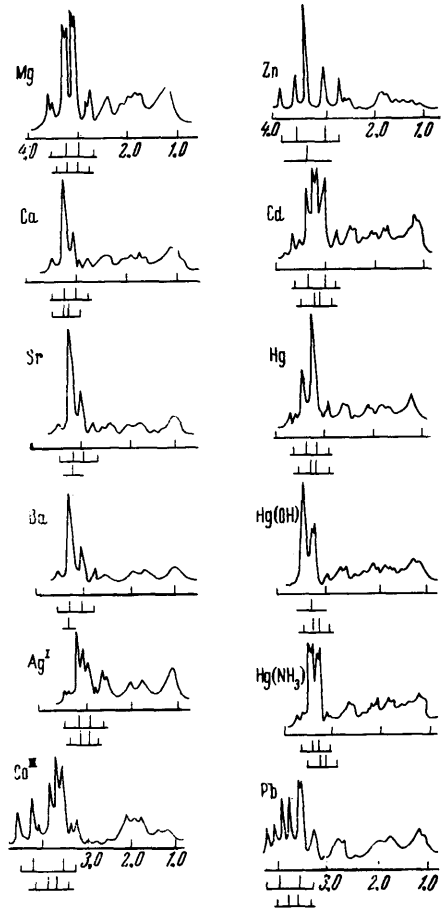


Figure 8. Characteristic spectra of metal complexes of CDTA.

The cobalt(III) and rhodium(III) complexes of monoamine derivatives (MIMDA, IMDA, and NTA) [53–57], diamine derivatives (EDDA, ED3A, HEDTA, EDTA, PDTA, BDTA, and CDTA) [58–67], and DTPA [99] have been investigated. The metals form with each ligand complexes of similar structure. Accordingly, their PMR spectra are also similar.

The spectra of the complexes with monoamine derivatives [53–56] show the AB quartets due to the protons of the acetate groups. In the spectra of the IMDA complexes, the AB quartets are broadened or split owing to the spin–spin interaction with NH protons. The signals of the NH groups are observed immediately after the solutions have been prepared. After the exchange with deuterium (D_2O), the signals disappear and the spectrum becomes simpler.

The formulae of the rhodium and cobalt complexes are isolated and their spectroscopic parameters are given in Table 8. The configurations are designated as follows:

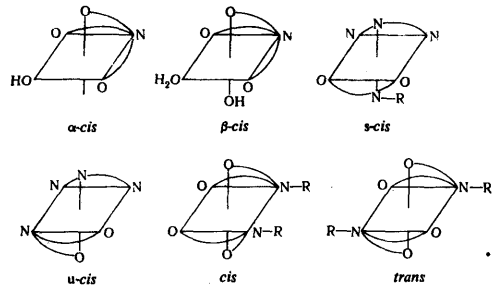


Table 7. Spectroscopic parameters of metal complexes of BDTA and CDTA. [26]

M^{n+}	BDTA						CDTA			
	methylene			methylidine	methyl		methylene			methylidyne
	δ	δ_{AB}	J^*_{AB}	δ	δ	J	δ	δ_{AB}	J_{AB}	
K_4	3.19	0.14	15.9	2.82	1.12	6.3	3.19	0.24	16.4	2.60
Mg	3.22 3.27	0.52 0.1	0.1 —	2.86 —	1.05 —	6.8 —	3.10 3.11	0.30 0.39	16.2 17.2	2.36 —
Ca	3.21 3.24	0.44 0.25	17.4 16.5	2.81 —	1.09 —	6.6 —	3.11 3.19	0.37 0.14	16.3 16.8	2.41 —
Sr	3.18	0.38	17.5	2.75	1.08	6.6	3.12 3.22	0.37 0.1	16.2 —	2.45 —
Ba	3.16	0.1	—	2.72	1.08	6.8	3.12 3.25	0.39 0.1	16.1 —	2.54 —
Zn	3.32 3.39	0.51 0.1	17.7 —	2.97 —	1.09 —	6.9 —	3.25 3.35	0.82 0.1	17.9 —	2.55 —
Cd	3.19 3.22	0.44 0.43	17.3 16.6	2.9 —	1.13 —	6.8 —	3.12 3.14	0.18 0.51	16.4 16.9	2.44 —
Pb	3.73 3.77	0.32 0.20	17.1 16.5	3.51 —	1.22 —	7.0 —	3.68 3.72	0.40 0.60	16.3 16.4	2.77 —
Hg	3.26 3.30	0.35 0.36	17.5 16.4	3.04 —	1.15 —	6.8 —	3.17 3.32	0.1 0.4	16.0 —	2.57 —
Ag	3.24	0.1	—	2.98	1.10	6.9	3.03 3.07	0.48 0.27	17.4 25.5	2.56 —

*Here and henceforth J is quoted in Hz.

The spectra of the *trans*-configurations of the 1 : 2 complexes and the s-*cis*-configurations of the 1 : 1 complexes show only one AB quartet and those of the *cis*- and u-*cis*-configurations show two AB quartets. In the spectra of the 1 : 2 complexes, the singlet corresponds to the free-carboxy-group. This is also indicated by the shift of the singlet towards higher fields as the pH of the solution is increased. Complexones with a tertiary nitrogen atom (NTA and MIMDA) give rise only to the *trans*-configurations owing to steric requirements.

The trend in the H_A and H_B proton shifts in the spectra of substituted IMDA can be accounted for on the basis of the magnetic anisotropy of the C–N bonds [57]. In the *trans*-complexes, substitution of the amino-proton by a CH_3 group leads to a greater screening of the H_A proton and to a smaller screening of the H_B proton. The *cis*-complex gives rise to a signal in higher fields than the corresponding *trans*-complexes.

In the cobalt complexes of diamine derivatives, the glycinate rings can be of two types: polar (out-of-plane) and equatorial (in-plane). Depending on this, one or two acetate groups at the nitrogen atom are bound in the complex, being designated by R_1 and R_2 for the polar groups and by G_1 and G_2 for the equatorial groups. The ring in which two nitrogen atoms are linked is designated by the letter E.

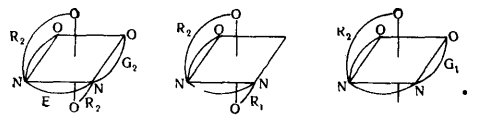


Table 8. Chemical shifts in the spectra of the cobalt(III) and rhodium(III) complexes of NTA, MIMDA, and IMDA. [55,56]

Complex	δ_A	δ_B	δ_R	J_{AB}	J_{NH-H_A}	J_{NH-H_B}
αK [Co (NTA) (OH) (OH_2)]·$2H_2O$	4.60	3.89	3.97	16.1	—	—
β-K [Co (NTA) (OH) (OH_2)]·$3H_2O$	4.34	3.75	3.91	16.1	—	—
Co (NTA) $(OH_2)_2$	4.41	3.79	4.11	16.5	—	—
Rh (NTA) $(OH_2)_2$	4.46	4.11	4.23	16.3	—	—
trans-H [Co $(HNTA)_2$]·$2H_2O$	4.34	4.11	4.51	17.6	—	—
trans-H [Rh $(HNTA)_2$]·$2H_2O$	4.30	4.16	4.55	17.5	—	—
trans-Co $(IMDA)_2^-$	4.42	3.61	9.0	17	—	—
trans-H [Rh $(IMDA)_2$]·$3H_2O$	4.25	3.55	8.25	17.4	7.6	1.5
after exchange	4.23	3.34	—	17.5	—	—
trans-$(Co (MIMDA)_2]^-$	4.25	3.86	3.17	17	—	—
trans-H [Rh $(MIMDA)_2$]·$2H_2O$	4.09	3.82	3.25	17.1	—	—
cis-$[Co (IMDA)_2]^{2-}$	4.24	3.26	7.6	17	—	—
	4.00	3.27	—	17	—	—
cis-H [Rh $(IMDA)_2$]·$2H_2O$	3.98	3.47	—	16.8	—	—
	4.28	3.44	—	17.9	—	—
s-cis-[Co (dien) (IMDA)]$^+$	4.29	3.45	—	17	—	—
s-cis-[Co (dien) (MIMDA)]$^+$	4.19	3.69	2.99	17	—	—
u-cis-[Co (dien) (IMDA)]$^+$	4.45	3.47	7.0	17	—	—
	4.35	3.41	—	17	7.8	1

Cobalt complexes of ED3A containing a monodentate ligand residue (Cl^- and NO_2) [58], the isomeric forms of complexes containing the EDDA and $AEIDA^X$ residues and bidentate ligand residues [CO_3^{2-}, ethylenediamine (en), oxalate (ox), and malonate (mal) [59-63]], and complexes of the type Co(HY)X and Co(Y)X, where Y =EDTA, PDTA, and HEDTA [26,64], have been synthesised.

The study of the PMR spectra established the number of polar and equatorial glycinate rings on the basis of the number of bands in the spectrum [60,62,65] and proton–deuterium exchange involving the CH_2 group [61] and permitted the assignment of the bands in the spectra.

Table 9 lists the possible forms of the complexes with diamine derivatives, the shifts of the H_A and H_B protons in rings of different types, and the positions of these signals in the spectra of the hexa- and penta-dentate EDTA and HEDTA complexes. Their comparison shows that in the cobalt(III) spectra the H_A and H_B protons in each type of glycinate ring give rise to characteristic band positions, varying in the range 4–4.2 and 3.1–3.4 for R_1, 4.2–4 and 4–3.9 for R_2, and 3.9–4.2 and 3.7–4 for G_2. The differences between the H_A and H_B chemical shifts remain approximately constant: 0.7–0.9 for R_1, 0–0.2 for R_2, and 0–0.2 for G_2. The spectra corresponding to the R_2 and G_2 rings are similar.

These values may be useful for the elucidation of the structure in those cases where isomers can be formed.

Thus two glycinate rings of type G_2 and one ring of type R_2 ($\delta AB = 0$) are observed in the complexes with the pentadentate EDTA and HEDTA residues, which confirms the *trans*-position of the NO_2 groups relative to the acetate group in these compounds. The degeneration of the CH_2 quartet of the R_2 ring to a single is due to the small chemical shift difference between the H_A and H_B protons [66].

Table 9. Positions of the signals due to the CH_2 protons in various rings of the cobalt(III) and rhodium(III) complexes of diamine derivatives*.

Complex	H_A	R_1	H_B	H_A	G_1	H_B	E**	Refs.
trans-[Co (en) EDDA]$^+$	4.19		3.37	—		—	3.10	62
trans-[Co (ox) EDDA]$^-$	4.28		3.33	—		—	—	59
trans-[Co (mal) EDDA]$^-$	4.20		3.25	—		—	—	59
cis-[Co (en) EDDA]$^+$	4.02		3.15	—	3.71	—	—	59
cis-[Co (ox) EDDA]$^-$	3.92		3.09	—	3.56	—	—	59
cis-[Co (mal) EDDA]$^-$	3.99		3.09	—	3.48	—	—	59
[Co (ED3A) NO_2]$^-$	4.16		3.42	3.96	G_2	3.88	—	59
[Co (EDTA) $Cl]^{2-}$	4.27		3.28	4.02		3.82	—	26
[Rh (EDTA) $Cl]^{2-}$	4.50		3.85	4.14		3.89	—	67
[Rh (EDTA) $Cl]^{2-}$	4.23		3.75	4.20		4.09	—	67
trans-[Co (en) (DMeEDDA)]$^+$	4.11		3.69	—		—	2.83	62
trans-[Co (en) (DEtEDDA)]$^+$	4.10		3.62	—		—	2.78	62
[CoEDTA]$^-$	3.96	R_2	3.88	3.91		3.58	3.85	67
[RhEDTA]$^-$	4.07		3.97	4.00		3.83	3.71	67
[Co (EDTA) $NO_2]^{2-}$		4.12		4.11		3.86	—	59
		4.2		4.26		3.78	—	59
[Co (HEDTA) NO_2]$^-$		4.13		4.09		3.87	—	59
				4.36		3.46	—	
cis-[Co (AEIDA) en]$^+$	4.21		4.05	4.18		4.02	—	59
Co (PDTA)$^-$	4.11		3.41		3.70		—	26
	3.91		3.53	4.03		3.82	—	
[CoBDTA]$^-$	4.02		3.36	3.87		3.59	—	26
	4.14		3.43	3.96		3.86	—	
[CoCDTA]$^-$	4.25		3.37	3.83		3.52	—	26

*δ in p.p.m.; J = 11–19 Hz.

**The chemical shifts of the ethylene protons for the remaining complexes are not quoted in the original papers.

In the analogous EDTA complex with a chloride ion, the latter is located in the plane [of the ring ?] (only the R_1 ring is observed).

Complexes of EDDA and its *C*-substituted derivatives with cobalt and neutral ligands have been investigated. For the *trans*-coordination of EDDA, the acetate groups are identical and there is only one AB quartet (due to the R_1 ring), while in the *cis*-isomer there are two types of acetate rings (R_1 and G_1) and the spectrum contains an AB quartet and a singlet.

The E ring of the *trans*-complex has two equivalent proton sets, each of which contains equatorial (eq) and axial (ax) protons giving rise to A_2B_2 splitting. The chemical shifts in the spectra of these compounds have been accounted for on the basis of the magnetic anisotropy of the C–N bond [57]. The application of molecular models to cobalt complexes showed that the angles between the $C-H_{eq}$ and $C-H_{ax}$ bonds on the one hand and the molecular axis on the other are different, varying on alkyl substitution from 80° for H_{eq} and 40° for H_{ax} in the EDDA complex to 65° and 85° for the corresponding protons in the DMeEDDA and DEtEDDA complexes, which leads to a change of the chemical shift of the ethylene protons from 3.10–3.12 p.p.m. to 2.83–2.78 p.p.m.

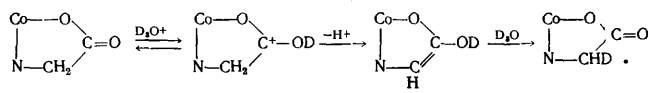
One can also investigate the effect of C–N bonds on the protons of the glycinate ring. The protons located on the

same side of the ring as the amino-proton or the substituent are designated by H_A and those on the other side by H_B. These protons are symmetrical in relation to the C–N bond in the R ring and are screened by this bond to an equal extent, but H_B is located above the C–N bond in the ring, while H_A is at an angle of 40° relative to the C–N axis. Therefore H_B should be screened more than H_A. Such a situation arises in the EDDA complex. If the proton linked to the nitrogen atom is substituted by an alkyl group, the protons of the R ring are distributed in a different way: H_A at right angles and H_B at an angle of about 35° relative to the bond axis. Under these conditions H_A is screened and H_B descreened. Indeed in the DMeEDDA and DEtEDDA complexes, the signal due to H_A shifts towards higher fields and that due to H_B towards lower fields.

Probably the change in the disposition of the H_A and H_B protons is responsible also for the increase of the difference $\delta A - \delta B$ in the spectra of the cobalt complexes of PDTA, BDTA, and CDTA.

To elucidate the structures of the complexes, one also employs the ability of the acetate group protons located in the vertical planes to undergo exchange with deuterium of heavy water in an acid medium at high temperatures, which leads to a gradual decrease of the intensity and the final disappearance of the signal due to these protons [67].

The study of the kinetics of the exchange of the protons of the acetate groups led to a tentative mechanism of the exchange reaction involving the formation of an intermediate enolic form of the complex:



These investigations also made it possible to determine the relative positions of the CH_2 protons in the complexes [58].

The study of the PMR spectra of rhodium complexes of EDTA established the mechanism of the complex formation process as a function of the solution pH and the number of EDTA binding groups employed in the complexes $Rh(EDTA)(H_2O)$, $RhH(EDTA)X$, and $RhH_2(EDTA)X_2^-$¶, where X = Cl or Br. [68] In the first complex, the composition and the number of EDTA binding sites employed change with increase of the pH:

$$\underset{(I)}{Rh(HY)(H_2O)} \leftrightarrow \underset{(II)}{RhY} \leftrightarrow \underset{(III)}{RhY(OH)^{2-}}.$$

The number of binding sites employed is five in complexes (I) and (III) and six in complex (II); this is confirmed by the presence in the spectra of the first two complexes of signals due to the free acetate group, which are displaced as the pH is varied. The number of free and bound groups was determined from the ratio of the signal areas (1 : 3). Under conditions close to neutrality, the signals of the free acetate groups were not observed.

The signals of the free acetate groups were also noted in the spectra of the complexes $Rh(HY)X^-$ and $Rh(H_2Y)X_2^-$, the ratio of the bound and free groups being 3 : 1 and 2 : 2 in the first and second cases respectively, corresponding to penta- and tetra-dentate EDTA residues. In the last case, the presence of only two AB quartets shows that the EDTA oxygen atoms are in the *trans*-positions, which is consistent with the presence of the R_1 rings in the complexes $[Rh(EDTA)Cl]^{2-}$ and $[Rh(EDTA)Cl_2]^{3-}$.

¶ $RhY(H_2O)$, $Rh(HY)X$, and $Rh(H_2Y)X_2^-$.

Platinum(II) and palladium(II) complexes differ from those of cobalt(III) and rhodium(III) by the fact that the metal coordination number in them is four. In the PMR spectra of the majority of platinum and palladium compounds, AB quartets are also observed [69–71]. The number of binding sites in the complexones (IMDA, MIMDA, and NTA) employed in the 1 : 1 platinum and palladium complexes does not exceed three; the oxygen atoms of the acetate groups are located in the *trans*-positions and are equivalent (one AB quartet). The angles between the C–H_{AB} and C–N bonds were determined from the chemical shifts and the spin–spin coupling constants of the H_A and H_B protons: $\theta_{HA} = 80°$ and $\theta_{HB} = 155°$.

After the addition of ammonia to the palladium complexes of IMDA and MIMDA, initially one water molecule is substituted and then one and two oxygen atoms of the complexone are displaced.

The 1 : 2 complexes were found to have *cis*- and *trans*-isomers for IMDA and only the *trans*-isomers for MIMDA and NTA. The chemical shifts of the platinum and palladium complexes investigated are presented in Table 10, which also includes the constants for spin–spin coupling to the magnetic nuclei of platinum.

Table 10. Spectroscopic parameters of the platinum and palladium complexes of IMDA, MIMDA, and NTA. [69–71]

Complex	δ_A	δ_B	δ_R	J_{AB}	J_{PtH_A}	J_{PtH_B}	J_{Pt-R}
[HPt(MIMDA)Cl]·2HCl	4.53	4.08	3.17	17.1	5.5	33.5	27.1
[KPt(IMDA)Cl]·2HCl	4.5	3.76	—	17.5	5.5	35.5	—
Pd(MIMDA)OH·H_2O	4.31	3.35	2.86	16.1	—	—	—
Pd(MIMDA)NH_3	4.25	3.42	2.83	16.1	—	—	—
Pd(IMDA)(OH_2)·H_2O	3.93	3.42	—	16.0	—	—	—
Pd(IMDA)(NH_3)	3.71	3.18	—	16.1	—	—	—
Pt(NTA)	4.58	4.44	4.09	16.5	18.0	37.0	10.5
Pt$(H_2NTA)_2$	3.87	3.78	4.02	15.9	28.0	18.5	26.5
Pd$(H_2NTA)_2$	—	—	3.78	—	—	—	—
PtH_2(IMDA)$_2$	3.78	3.42	—	16.8	43.0	22.0	—
	3.56	3.39	—	16.7	22.0	18.0	—
PdH_2(IMDA)$_2$	3.64	3.46	3.27	16.5	—	—	—

The PMR spectra of the platinum complexes hardly change with temperature and those of the palladium complexes of NTA show only one signal due to acetate protons, which can be accounted for by the averaging of the signals owing to rapid exchange (lability of M–O bonds). The increase of the lability of the bonds from platinum(II) to palladium(II) is consistent with the known rates of substitution reactions involving the complexes of these metals [72] and may be due to a weakening of the bonds in the palladium(II) complex. The latter is consistent with the shift of the acetate proton signal towards high fields relative to the signals in the spectra of the corresponding platinum complexes.

Mixed cobalt [73–78] and platinum(II) [79] complexes containing an aminoacid as one of the ligands have been studied. The aim of these investigations was to establish the absolute configuration of the complexes and to study the rate of proton exchange and of the mutarotation of the chelated aminoacids.

Some data on the structure of the complexes and the delocalisation of electrons on complex formation may be obtained by analysing the chemical shifts. The chemical

shift is determined by the screening constant, which may be represented by the formula

$$\sigma = \sigma_{dia} + \sigma_{para} + \Delta\sigma + \sigma_{ring} \quad (21)$$

where σdia is the local diamagnetic term, σpara the local paramagnetic term, $\Delta\delta$ represents the effect of the anisotropy of the neighbours, and σring represents the interatomic ring currents [80]. In a study of the proton resonance of acyclic compounds, only the first and third terms should be taken into account.

By considering a series of complexes of various metals with the same ligand, it is possible to distinguish three cases. (1) $\sigma_{dia} > \Delta\delta$; the chemical shift is determined by σ_{dia}, which is a function of electron density. Since complex formation involves the delocalisation of electrons with decrease of electron density at the ligand, a correlation should be observed between z/r or the ionisation potential and the shift towards lower fields. (2) $\sigma_{dia} \simeq \Delta\delta$; the correlation between the chemical shift and the electronegativity breaks down and the signal shift on complex formation may be close to zero if σ_{dia} and $\Delta\delta$ have opposite signs. (3) $\sigma_{dia} < \Delta\delta$; the chemical shift is determined by the symmetry of the complex and is independent of z/r or I for the same symmetry.

Comparison of the chemical shifts of the complexone anions and various complexes shows that in the spectra of certain metal (Li, Na, Mg, Ca, Sr, and Ba) complexonates no signal shift is observed or only a slight shift towards higher fields. This can be accounted for by the fact that the degree of descreening on formation of the metal complexes is caused by the disposition [81] assumed by the complexone atoms on complex formation.

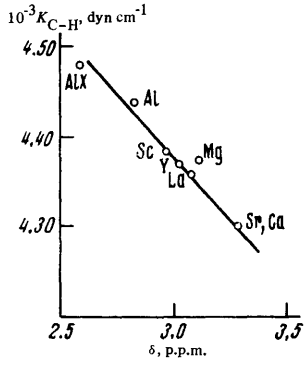


Figure 9. Relation between the chemical shift and the valence-force constant of the C–H bonds for AlX and MX_2 complexes (M = Al, Mg, Ca, Sr, Sc, Y, or La).

In the spectra of the majority of the complexes of the remaining metals, there are signal shifts towards lower fields. If complexes of identical symmetry are formed, the $\Delta\delta$ term will remain approximately constant and the increase of the shift towards lower fields is due to the increase of the delocalisation of electrons on bond formation.

For the NTA complexes, a correlation between the chemical shift and the bond force constant was observed (Fig. 9) [82]. For rhodium and cobalt complexes of the same structure, the chemical shift of the acetate protons in monoamine derivatives and of the ethylene protons in diamine derivatives was found to increase from rhodium to cobalt, which is consistent with the increase of the ionic and ionisation potentials.

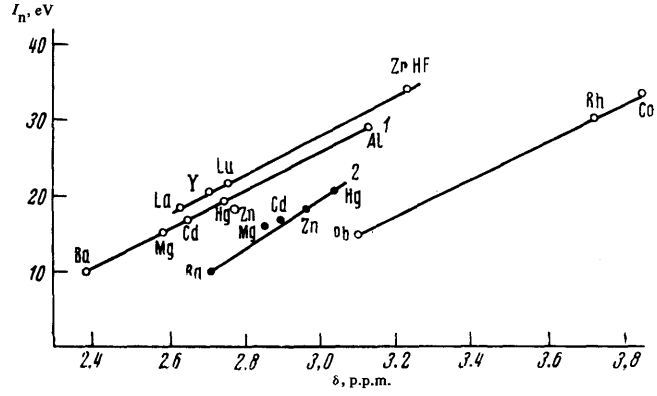


Figure 10. Relation between the ionisation potential of the metal and the chemical shift for EDTA (lines *1*) and BDTA (line *2*) complexes.

Three correlations were found between the ionisation potential I_n, where n is the charge of the metal, and the chemical shift of the EDTA ethylene protons for three groups of metals: (1) lead, rhodium, and cobalt; (2) lanthanum, yttrium, lutetium, zirconium, and hafnium; (3) barium, magnesium, mercury, zinc, and cadmium (Fig. 10). The correlation indicates an identical symmetry of the complexes within the limits of each group and a change in symmetry (with a change in $\Delta\delta$ by a constant amount) on passing from one group of metals to another.

In the first group there is an octahedral symmetry with two nitrogen atoms and two oxygen atoms of the carboxy-groups located in the same plane with the metal atom and two oxygen atoms of the acetate group located in the plane at right angles (a coordination number of six). The formation of polyhedra of lower symmetry (C_1, C_2) with a coordination number greater than six [83,84], in which only the nitrogen atoms are in the same plane as the metal, is characteristic of the second group of metals. The third group includes metals with a noble gas outer shell, in the complexes of which the coordination number may be less than six. These complexes have presumably a *trans*-structure with rapid exchange of the nitrogen atoms along the vertical axis and with the oxygen atoms of the carboxy-groups located in the same plane as the metal ion.

A correlation between the stability constants and the chemical shifts is not always observed. Nor is a linear correlation observed between the stability of the EDTA complexes and the rate of intrachelate and interchelate exchange: with increase of the stability constants, there is both an increase and a decrease of the rate of exchange.

A linear correlation between the stability of bivalent metal complexes and the rate of exchange is observed for the base-catalysed substitution of CH_2 protons in the

acetate residues by deuterium: the rate of proton exchange increases with the stability of the complexes and of the ionisation potential (Fig. 11) [85].

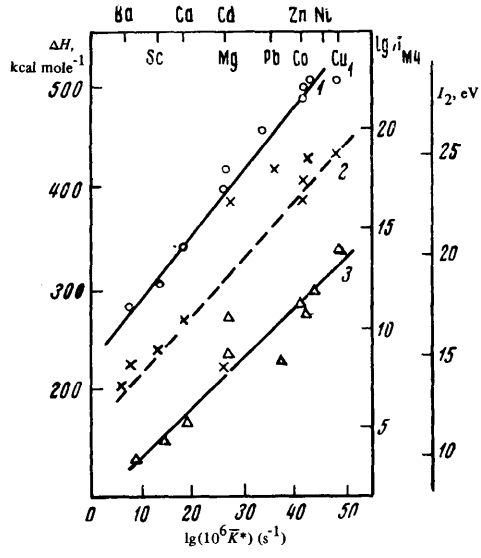


Figure 11. Correlation between the thermodynamic characteristics [1) heat of formation of gaseous MY ions; 2) $\lg K_{MY}$; 3) ionisation potentials] and the rate of proton exchange.

On formation of mixed hydroxo-complexes with substitution of one acetate group by a hydroxide ion, the rate of proton exchange decreases [$Zn(EDTA)(OH)^{2-}$]. If a mixed hydroxo-complex is formed without the dissociation of the linkage with the acetate groups [$Cd(EDTA)(OH)^{2-}$], the rate of proton exchange remains unchanged. Thus the rate of proton exchange serves as an indicator whereby it is possible to establish the structure of the mixed hydroxo-complexes.

The chemical shifts of the acetate protons and their variation in a series of BDTA complexes with various metals are approximately the same as for the EDTA complexes (Fig. 10).

In the CDTA complexes, the chemical shift is almost independent of the metal (apart from the lead complexes). The absence of a dependence on z/r or the metal ionisation potentials can be explained by approximately equal contributions of inductive (σ_{dia}) and long-range ($\Delta\delta$) effects. This is confirmed by similar differences between the chemical shifts of the H_A and H_B protons, the latter being determined by long-range screening [26].

2. Paramagnetic Complexes

The paramagnetic complexes differ from the diamagnetic complexes by higher contact and pseudocontact shifts and considerable changes in the relaxation times on complex formation [47]. Nickel(II), cobalt(II), and copper(II) complexes of aminoacids and complexones and EDTA complexes of uranium(IV) and paramagnetic lanthanide ions have been investigated.

The spectra of complexes with ligands containing NH_2 and NH groups, show lines in the region of high fields (between +50 and +200 p.p.m.), which are attributed to the protons of these groups. It has been shown that these protons exchange with the water protons at the rate of 1×10^3 s^{-1}. The water molecules bound to the ion do not give rise to a separate line (rapid exchange). The majority of lines in weak fields are attributed to the protons of the CH_3, CH_2, and CH groups bound to the nitrogen atom.

The signals of the protons in the CH_2 groups bound to COO^- groups are displaced towards higher fields. The observed directions of the shifts can be accounted for by a contact interaction on formation of the covalent bond [47,86].

However, pseudocontact interaction (the effect of anisotropy) also plays a considerable role. The presence of the CH_3 group in the sarcosine complexes of nickel leads to a disposition of the chelate ring such that the two C–N bonds involving methylene groups form different angles with the Ni–N–C plane, which results in a splitting of the methylene proton signal into two lines (–100 and –40 p.p.m.). In the corresponding glycinate complex there is only one resonance of CH_2 groups, which can be explained by the planarity of the glycinate ring [86].

In complexes with polydentate ligands, a rigid structure may be formed, incorporating several rings which are not planar, which should lead to a splitting of the CH_2 proton signals.

Proton resonance of the nickel(II) complexes of tridentate complexones and nickel(II) and cobalt(II) complexes of tetra- and hexa-dentate complexones has been investigated [86,87]. 1 : 1 complexes with iminodiacetic acids and NTA were shown to have the *cis*-configuration. The following ratios of the *cis*- and *trans*-configurations were found in the complexes with two ligand species: 80 : 20 for IMDA, 40 : 60 for MIMDA, and < 10 : 90 for NTA. [88]† In complexes with two tetradentate ligand species (HIMDA and NTA), the number of binding sites of the ligand employed decreases to 3. The lifetimes of the Ni–N and Ni–O bonds have been determined. In complexes with one NTA residue, the exchange is faster than in the complexes with two NTA residues, which can be explained by the fact that the substitution of water molecules is faster than the substitution of the acetate group. The rate constant is of the order of 10^5 s^{-1}. In $Ni(IMDA)_2^{2-}$ and $Ni(MIMDA)_2^{2-}$, the rate of exchange is lower than in the NTA complex, owing to the absence of a free acetate group [56] ($\bar{k} < 10^3$ s^{-1}) [88].

The spectra of the nickel(II) and cobalt(II) complexes of hexadentate ligands depend on the pH of the solution: the bands are displaced and their width changes. The spectra of the cobalt complexes contain sharper lines and their structure is more complicated, which can be explained by a lower rate of exchange in these complexes [86].

In the spectra of all the metal compounds with complexones investigated, the signals of the CH_2 group linked to a nitrogen atom are split into two components, which can be accounted for by the anisotropy of the linkage (different angles between the Ni–N–C plane and the CH_2 protons). The difference between the chemical shifts of the CH_2 protons increases in the spectra of complexes with six-membered rings compared with complexes having five-membered rings. The explanation may be that the angles between the Ni–N–C plane and the C–H vector

† *cis*- and *trans*- in relation to the oxygen atoms.

differ more on formation of six-membered rings. All these conclusions are consistent with X-ray diffraction studies [89,90,91] and with studies on the PMR spectra of the diamagnetic complexes (see p. 271). The shift of the N–CH_2 protons and the angle between the Ni–N–C plane and the C–H vector have been found to be correlated (Fig. 12).

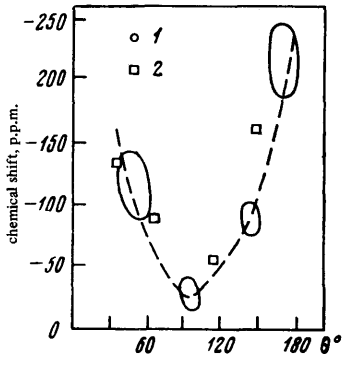


Figure 12. Correlation between the shift of the CH_2 proton signals and the NiNC–H angle: 1) angles determined from the model; 2) X-ray diffraction data.

The study of mixed complexes containing an EDDA residue and an aminoacid established the conformation of the glycine ring in the unsubstituted and methyl-substituted glycinate complexes: the number of binding sites of the tridentate aminoacids employed in the mixed complexes was found to be reduced, the stereochemistry of the mixed complexes was established, and stereoselective coordination of the aminoacids in the mixed complexes was found [92].

Mixed complexes of asymmetric aminoacids give rise to diastereoisomers, which can be detected in the PMR spectra.

Interesting studies have been made on complex-formation equilibria with simultaneous investigation of the structure of the complexes in the cobalt(II)–histidine system [93]. Fig. 13 illustrates the variation of the contact shift of the protons in water and histidine,

$$(\overset{+}{N}H_3\text{—}\underset{\displaystyle COOH}{\underset{|}{C}}H(\alpha)\text{—}CH_2(\beta)\text{—}),$$

as the pH of the solution is varied. At a low pH, there is a greater contact shift of the water protons, while the histidine protons do not exhibit a shift relative to the free ligand, i.e. there is no complex formation. With increase of the pH, the signals of the $H\alpha$ and $H\beta$ histidine protons are displaced, which indicates coordination via the nitrogen atom and the COO^- group. At pH > 4, the contact shift of the water proton signals decreases with a simultaneous increase of the contact shift of the signals due to the protons in the imidazole ring and at pH > 6 the position of the water proton signal becomes the same as in pure water. This shows that under these conditions water does not enter the inner sphere of the complex.

Four complexes were discovered in the system, in which the linkages are formed either with the COO^- group alone or with the COO^- group and one or two nitrogen atoms. In the latter case, there is a transition from octahedral to tetrahedral configuration [93].

The hydration and structures of certain copper(II) aminoacid complexes have been investigated [94]. The hydration numbers of copper and the distances between the copper atom and the oxygen atoms of water in complexes with aminoacids and in the normal and protonated EDTA complexes were determined from the relaxation time of the water protons (Table 11).

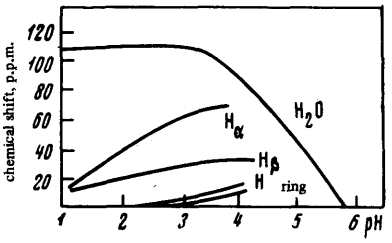


Figure 13. Variation of the contact shifts of the proton signals of water and histidine ($H\alpha$, $H\beta$, H_{ring}) with the pH of the solution.

The spectra of EDTA complexes with paramagnetic lanthanide ions (cerium, neodymium, praseodymium, and samarium) show one AB quartet due to the methylene protons and a singlet due to the ethylene protons. The presence of one AB quartet can be accounted for either by the equivalence of the methylcarboxyls or by a rapid exchange between them. The latter is more likely. In a mixture of complexes of two lanthanides, two sets of signals due to these complexes are observed. The relative concentrations of the complexes were determined from the relative intensities and the stability constants were calculated from the exchange equilibrium constants [97]. The constants obtained agree with the values quoted in the literature [3].

Table 11. Cu–OH_2 distances in complexes with aminoacids and EDTA.

Ligand	$[CuA(H_2O)_4]^+$ Cu–OH_2, Å		$CuA_2(H_2O)_2$ Cu–OH_2, Å	
	soln.	crystal	soln.	crystal
Glycine	2.12		2.29	
α-Alanine	2.18		2.34	
β-Alanine	2.16	2.20*	2.26	2.43*
Sarcosine	2.16		2.28	
Dimethylglycine	2.21		2.39	
	$[CuA(H_2O)]^{2-}$		$[CuHA(H_2O)_2]^-$	
EDTA	2.03	2.08**	2.08	

*Refs. 95 and 96.

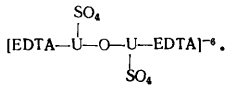
**In $Ni(H_2EDTA)H_2O$ which is isomorphous with the copper(II) complex [89].

In the uranium(IV) complex of EDTA in the presence of sodium sulphate above 27 °C, the U–O bonds are labile and the U–N bonds are non-labile, while below 27 °C the U–O

bonds also become non-labile [98]. This is reflected in an additional splitting of the signals due to the methylene and ethylene protons. Measurements of the rate of exchange and inversion at different temperatures and of the activation parameters for these processes showed that the ethylene ring undergoes inversion without dissociation of the metal–ligand bonds ($\Delta G = 10.22$, $\Delta H = 10.8$, and $\Delta S \simeq 0$).

The study of the spectra at different pH revealed two types of complexes (at pH 0–3 and at pH > 6). At lower pH values, the signals due to free EDTA are also observed.

The complex formed in the acid region is a monomer with a distorted cubic structure. At pH > 6, dimeric species with an oxygen bridge and incorporating sulphate groups are formed:



The structure of the monomeric complex was deduced by analysing the chemical shifts on its formation [92].

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Institute of General and
Inorganic Chemistry,
Academy of Sciences of
Ukrainian SSR, Kiev

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Chemical Reactions of Cobaltocene and Nickelocene

E.V.Leonova and N.S.Kochetkova

This review deals with the comparative chemical characteristics of metallocenes containing Group VIII metals in the Third Period of the Periodic System, namely cobaltocene, nickelocene, and their derivatives. The common features of their chemical properties and the differences between them have been elucidated. The capacity of cobaltocene and nickelocene to form complexes with electron-accepting agents is discussed.
The bibliography includes 200 references.

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I. INTRODUCTION

π Complexes with a sandwich structure, the first representative of which is ferrocene, have been a truly inexhaustible store of interesting problems and puzzles for a generation of investigators. The similarity of the structures and similar principles of the formation of chemical metal – cyclopentadienyl (CP) ligand linkages are responsible for the similarity of the physicochemical properties of metallocenes. However, the nature of the central metal atom should have a significant influence on the metal – ligand bond, causing a corresponding change in the properties of the "sandwich".

In the Third Period, Group VIII of the Periodic System contains three elements (iron, cobalt, and nickel) each of which forms the corresponding "sandwich" compound. The variation of the physicochemical properties of these complexes on passing from iron to nickel is interesting. In view of the large number of reviews and monographs on the chemistry of ferrocene and other π complexes with a sandwich structure[1–10], this review deals mainly with experimental studies on the chemistry of nickelocene, cobaltocene and the cobalticenium cation (up to 1972), the chemical properties of ferrocene being considered only for the purposes of comparison.

The review does not discuss the catalytic properties of these metallocenes and their other possible applications.

II. SUBSTITUTION REACTIONS OF THE CARBON ATOMS OF COBALTOCENE AND NICKELOCENE.

One of the simple chemical proofs of the non-benzenoid aromatic nature of metallocenes is the absence of Diels – Alder reactions with maleic anhydride and reactions with iron(II) chloride as well as the resistance of these compounds to hydrolysing agents. Another important piece of chemical evidence for the aromaticity of these systems is the capacity to undergo substitution reactions.

Neither cobaltocene nor nickelocene form ferrocene by reacting with $FeCl_2$.[11] However, nickelocene is not decomposed by water and cobaltocene is converted into the stable cobalticenium cation[11]. However, whereas electrophilic substitution reactions are typical for ferrocene[1–10], all attempts to acylate, arylate, and metallate nickelocene[10] and also to sulphonate, nitrate, acylate, and arylate cobalticenium picrate[10] under conditions close to those of the analogous ferrocene reactions were unsuccessful. Hitherto, the only known substitution reaction involving the hydrogen atoms of the cyclopentadienyl rings of the cobalticenium cation and nickelocene is the protophilic hydrogen isotope exchange reaction[12]:

$$(C_5H_5)_2M \rightarrow (C_5D_5)_2M\ (M=Fe;\ Co;\ Ni).$$

When nickelocene is treated with *N*-deuteriodiethylamine in the presence of lithium diethylamide, hydrogen isotope exchange takes place with the cyclopentadienyl ring of nickelocene[13, 14]. The rate of hydrogen isotope exchange involving nickelocene depends on the concentration of lithium diethylamide and, when the latter is 0.09 *N* in solution in *N*-deuteriodiethylamine at 25°C, the isotope exchange rate constant is 6×10^{-5} s^{-1}:

$$(C_5H_5)_2Ni \xrightarrow[Et_2NLi]{Et_2ND} (C_5D_5)_2Ni.$$

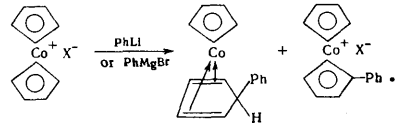
It is noteworthy that the protophilic hydrogen isotope exchange in ferrocene takes place under more severe conditions — in liquid ammonia in the presence of potassamide[15]. The rate constant for the replacement of deuterium in deuterioferrocene by protium in 0.02 *N* potassamide solution in liquid ammonia at 13°C is 9×10^{-4} s^{-1}. Under the same conditions, the rate constant for the exchange of deuterium in benzene is 3×10^{-5} s^{-1}. The data quoted show that in ferrocene and in benzene hydrogen atoms possess a much lower protophilic mobility than in nickelocene[12].

The kinetics of hydrogen isotope exchange between cobalticenium hydroxide and 10% sodium methoxide solution in *O*-deuteriomethanol at 50°C were also investigated and it was established that the rate constant for this reaction is 6.4×10^{-5} s^{-1}.[16] The degree of exchange is 80 – 90% of equilibrium value:

$$(C_5H_5)_2Co^+X^- \xrightarrow[MeONa]{MeOD} (C_5D_5)_2Co^+X^-.$$

The fact that a substitution and not an addition reaction occurs follows from a comparison of the ^1H NMR and infrared spectra of the initial and deuteriated compounds. The ^1H NMR spectrum shows in both cases a singlet with δ = = 5.85 p.p.m., and the infrared spectra of the deuteriated and the initial compounds are extremely similar[16].

It was also shown that in the reaction with phenyllithium or with phenyl-magnesium bromide, cobalticenium salts form, together with addition products, also a certain amount of a phenyl-substituted product[17]:



Other cobalt-containing metallocenes exhibit the chemical properties of aromatic systems. These compounds include cyclopentadienyl(tetraphenylcyclobutadienyl)cobalt[18, 19] and its unsubstituted analogue[20]. While the acylation reactions of these compounds have low yields (less than 1%[18, 19] and 5%[20] respectively), mercuration[20], the Mannich and Vilsmeier reactions[20], and substitution with lithium[20] take place readily. It is noteworthy that substitution of $C_5H_5CoC_4H_4$ takes place preferentially in the cyclobutadienyl ring[20].

The krypton electronic configuration obtains in these compounds. Analogous organonickel compounds, in particular (cyclopentadienyl-R_3-cyclopropenyl)nickel, exist. The three-membered ring can contain both aromatic[21] and aliphatic substituents[22]. An X-ray diffraction study of the compound $C_5H_5Ni(C_3Ph_3)$ has been carried out[23]. Possibly these compounds, like the cobalt-containing metallocenes, will show a tendency to undergo electrophilic substitution reactions.

III. REACTIONS IN THE SIDE CHAINS OF SUBSTITUTED COBALTICENIUM SALTS

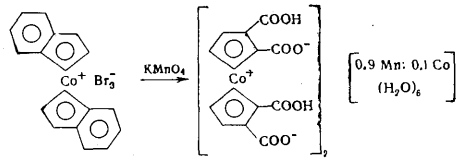
The possibility of carrying out reactions involving the side chains of substituted metallocenes (cobaltocene and nickelocene), other conditions being equal, arises primarily from the strength of the metal – ring bond. Nickelocene is known to enter readily into ligand exchange reactions. On the other hand, the nickelicenium cation and dication are extremely labile and are readily decomposed by atmospheric oxygen. No ligand exchange in aqueous solution at pH 1.99 takes place between cobalticenium perchlorate $(C_5H_5)_2CoClO_4$ and $^{60}Co(ClO_4)_2$.[24]

The cobalticenium cation is not decomposed by concentrated sulphuric and nitric acids[25, 26], but is ozonised when ozone is passed through its solution in acetic acid over a period of many hours[27]. These factors permitted a series of side chain reactions of substituted cobalticenium cations. Similar reactions are not known for the cation and dication derived from nickelocene.

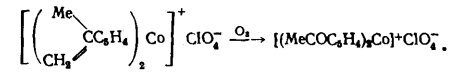
1, 1′-Dimethylcobalticenium perbromide was oxidised at 100°C with an aqueous alkaline solution of potassium permanganate[28]:

$$[Co(C_5H_4Me)_2]^+Br_3 + MnO_4^- \rightarrow [Co(C_5H_4COOH)_2]^-Br^+.$$

The dicarboxylic acid formed in this process was isolated as the bromide. A similar reaction was carried out with bis(indenyl)cobalt(III). 1, 2, 1′, 2′-Tetracarboxycobalticenium has been obtained as a mixed salt:



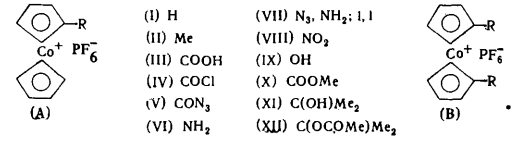
1, 1′-Di-isopropenylcobalticenium perchlorate has been ozonised[29]:



1, 1′-Diacetylcobalticenium has been characterised as the tetraphenylborate and the derivative with the anion of the Reinecke salt.

A mixture of cobalticenium (Ia), methylcobalticenium (IIa), and 1, 1′-dimethylcobalticenium (IIb) has been oxidised[30] with an alkaline solution of sodium permanganate to the corresponding carboxylic acids (III, A, B). The carboxy group was further converted into the acid chloride group (IV, A, B), an ester, an amide, and finally an acid azide (V, A, B). The Curtius rearrangement of the azide gave an amine (VI, A, B) and the 1-amino-1′-azido-compound (VII, B). Similar reactions are also known for ferrocenes[31]. However, in contrast to ferrocenylamine, the aminocobalticenium salt can be oxidised to the nitro-derivative (VIII, A)[30]. Moreover, the aminocobalticenium salt can be diazotised and azo-coupled[30]. Under these conditions, aminoferrocene is converted into the corresponding arylferrocenes[1].

The reaction of dicarboxycobalticenium hexafluorophosphate with alcohol in an acid medium leads to the corresponding ester (X, B)[30]. Moreover, 1,1′-di-(α-hydroxy-α-methylethyl)cobalticenium hexafluorophosphate (XI, B)[32] and the corresponding diacetate (XII, B)[32] were obtained from 1, 1′-di-isopropylcobalticenium hexafluorophosphate:



The infrared spectra of mono-substituted cobalticenium salts with the COOH, CON_3, and NO_2 substituents do not contain frequencies in the region of 1000 and 1100 cm^{-1},[30] while homoannular homologues of cobalticenium salts have spectra with frequencies in this region, resembling in this respect ferrocene derivatives[33].

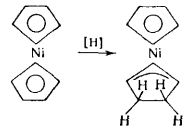
IV. REACTIONS INVOLVING ADDITION TO THE CYCLOPENTADIENYL LIGAND OF COBALTOCENE AND NICKELOCENE

1. Reductive Addition of Hydrogen.

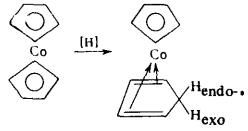
Ferrocene does not react with maleic anhydride[34] and is not hydrogenated in the presence of platinum[27] and Raney nickel[27, 35]. The hydrogenation of ferrocene was achieved under very severe conditions — in the presence of Raney nickel at 280 atm and 340°C,[36] but the iron—cyclopentadienyl ring bond was cleaved. For nickelocene †, this process takes place at 50°C in tetrahydrofuran (THF)

† The calculated standard free energies of formation of the biscyclopentadienyl compounds of iron, ruthenium, nickel, and manganese show that the reduction of these metallocenes by hydrogen with formation of the free metal and cyclopentadiene (CPH) or its hydrogenation products is more typical for nickelocene and ruthenocene than for ferrocene[37].

at 27 atm.[38] The reduction results in the formation of cyclopentadienylcyclopentenylnickel:



Nickelocene can also be reduced by sodium amalgam in ethanol[39,40]. Cobaltocene is reduced under similar conditions[41] with formation of cyclopentadienylcyclopentadienecobalt:



Its polarographic study showed[42] that cobaltocene is reduced more readily than nickelocene (-1.92 and -1.74 V respectively). It was established that the above electrochemical reaction of the π complexes is irreversible and that solvent protons are involved in it.

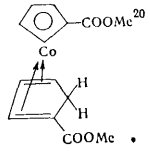
The conversion of $[(C_5H_5)_2Co]^+$ into $C_5H_5CoC_5H_6$ cannot be achieved by electrolysing neutral or alkaline aqueous solutions of a cobalticenium salt or by reduction with sodium amalgam, Devardov's alloy, and sodium dithionite[43]. $LiAlH_4(LaAlD_4)$ or $NaBH_4$ have been used for this purpose[43-47]. Probably attack by the hydride ion is a necessary condition for the conversion of the cobalticenium cation into cyclopentadienylcyclopentadienecobalt. Further interaction of cyclopentadienylcyclopentadienecobalt with lithium aluminium hydride does not entail a change in the structure and properties of the organocobalt compound[44]. It has been shown[42] that the reduction of the cobalticenium cation involves the initial reversible addition of an electron:

$$[(C_5H_5)_2Co]^+X^- + e \rightleftarrows (C_5H_5)_2Co,$$

and then the irreversible addition of hydrogen:

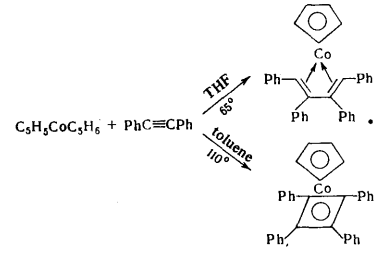
$$(C_5H_5)_2Co + \bar{e} + H^+ \rightarrow C_5H_5CoC_5H_6.$$

All the foregoing considerations apply to substituted cobalticenium salts. Treatment of 1, 1′-dimethoxycarbonylcobalticenium with $NaBH_4$ resulted in the formation of the corresponding organocobalt compound[20]:



If the last compound is not isolated and the reaction mixture formed is sublimed over a period of five days after removing the solvent, it is possible to isolate 1, 1′-dimethoxycarbonylcobaltocene in 47% yield[20]. By treating cyclopentadienylcyclopentadienecobalt with *N*-bromosuccinimide or benzaldehyde, it is possible to obtain cobalticenium salts[44]. The possibility of similar reactions involving nickelocene has not been investigated.

$C_5H_5CoC_5H_6$ and $C_5H_5NiC_5H_7$ are relatively unstable diamagnetic crystalline compounds. $C_5H_5NiC_5H_7$ decomposes on heating in nitrogen. The C_5H_6 group in $C_5H_5CoC_5H_6$ does not enter into the ligand exchange reaction with the cobalticenium cation in acetone solution[24]. When $C_5H_5CoC_5H_6$ is treated with diphenylacetylene[48] in THF at 65°C, the product is cyclopentadienyl-1, 2, 3, 4-tetraphenylbutadienecobalt, while in toluene at 110°C cyclopentadienyltetraphenylcyclobutadienylcobalt ‡ is formed[48,49]:



It is interesting to compare the results of the study of $C_5H_5CoC_5H_6$ and $C_5H_5NiC_5H_7$ by the ^1H NMR method.

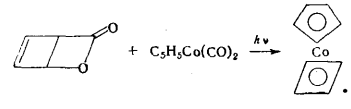
The authors[38] believe that the *endo*-protons are located in the region of the *d* orbitals of the nickel atom, so that they are strongly screened and there is a shift towards high fields (δ = 0.67 p.p.m.). The validity of this assignment has been confirmed by the appreciable broadening of the signal in a high field, which cannot be a consequence, as believed by the authors, of only the spin – spin splitting but suggests an interaction between the *endo*-protons and the nickel atom. If the suggested assignments are adopted, the disappearance of the 0.67 p.p.m. signal from the ^1H NMR spectrum of $C_5H_5NiC_5H_5D_2$ is evidence that the hydrogen adds to the cyclopentadienyl ligand and occupies the *endo*-position[38].

Green et al.[43], who were the first to analyse the ^1H NMR spectrum of $C_5H_5CoC_5H_6$, concluded that the signal in a higher field should be assigned to protons in the *endo*-position. The absence of this signal from the ^1H NMR spectrum of $C_5H_5CoC_5H_5D$ was regarded as evidence supporting the *endo*-addition of the hydrogen atom to the cyclopentadienyl ligand in the reduction of cobaltocene. This assignment is not inconsistent with the analogous interpretation of the infrared spectrum of this compound. The infrared spectra of compounds with similar structures ($C_5H_6CoC_5H_5$, $C_5H_6RhC_5H_5$, and $C_5H_6IrC_5H_5$) have an intense band due to the stretching vibrations of the CH group in the region of 2750 cm^{-1}. Such marked decrease of the frequency is caused, as suggested by Green et al.[43], by the interaction between the metal atom and a hydrogen atom in a favourable position, i.e. in the *endo*-position relative to the metal. The second absorption band of the CH group at 2950 cm^{-1} was assigned to an *exo*-hydrogen atom. The disappearance of the low-frequency band from the infrared spectra of substituted $R-C_5H_5CoC_5H_5$ derivatives was regarded as another piece of evidence supporting the above assignments.

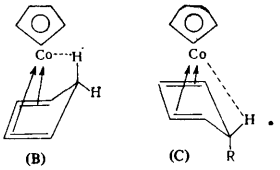
However, X-ray diffraction studies on benzoyl[52] and phenyl[53] derivatives of the above organocobalt compound showed that the group added occupies the *exo*-position, which the authors believe is not in conflict with the above interpretation of the infrared and ^1H NMR spectra[43].

The changes in the infrared and ^1H NMR spectra of $R-C_5H_5CoC_5H_5$ are associated with the differences in the

‡ The corresponding unsubstituted compound was obtained in a moderate yield on photolysing solutions of 2-oxabicyclo[2, 2, 0] hex-5-en-3-one and cyclopentadienyldicarbonylcobalt[20, 50]:



direction in which the methylene group deviates from the plane of the cyclopentadiene ligand. Whereas in the unsubstituted complex the methylene group is bent towards the metal (C), in the substituted derivative it is ben in the opposite direction[54] (D), The angular position of the CHR group greatly increases the distance from the metal to the formally *endo*-hydrogen atom (about 3.0 Å) and the Co – H interaction is weakened:



(B) (C)

Table 1. Parameters of the ^{1}H NMR Spectra of $C_5H_5CoC_5H_6$ and $C_5H_5NiC_5H_7$.

	δ, p.p.m.	Multiplicity	Relative intensity	Assignment	Solvent
a	5.12	1	5	C_5H_5	C_6D_6
	4.98	3	1	H^a	
	3.83	1	2	H^c	
	1.15	multiplet		H_{exo}	
	0.67[b]	multiplet		H_{endo}	
c	4.59	1	5	C_5H_5	C_6D_6
	5.25	3	2	H_3H_4	cyclohexane
	2.45	5—6	2¼	H_2H_5	
	2.68	3	¼	H^d_{endo}	
	2.01[e]	2	1	H_{exo}	

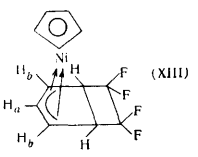
[a] 100 MHz.[38]
[b] There is no signal in the $C_5H_5NiC_5H_5D_2$ spectrum[38].
[c] 40 MHz.[43]
[d] The assignment has been made by analogy with that in Fischer's monograph[51].
[e] There is no signal in the $C_5H_5CoC_5H_5D$ spectrum.[43]

However, an alternative solution of the problem is possible. The methylene group in the substituted and unsubstituted compounds can deviate in the same direction (away from the metal) but to different extents from the plane of the butadiene fragment of the cyclopentadiene ligand. Then the ^{1}H NMR signal of $C_5H_6CoC_5H_5$ in a high field may be a consequence of the screening of one of the protons of the aliphatic group by the π electrons of the cyclopentadiene ligand in the complex[55]. In this case the high-field doublet should correspond to the *exo*-methylene hydrogen atom. The changes in the infrared spectra of the substituted and unsubstituted compounds are then determined by the changes in the angle between the plane of the butadiene fragment and the plane of the methylene group in the ligand. However, all these hypotheses require further X-ray diffraction study.

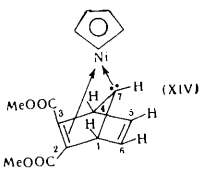
2. Addition of Alkyls, Alkenes, and Alkynes

The capacity of cobaltocene and nickelocene to add one and two hydrogen atoms respectively to the cyclopentadienyl ligand determines the type of interaction between these metallocenes and saturated and unsaturated compounds. Similar reactions are unknown in the chemistry of ferrocene. The degree of electronic unsaturation of the diene has a significant influence on the nature of its interaction with nickelocene.

The interaction of nickelocene with ethylene led to the isolation of cyclopentadienylcyclopentenylnickel[56]. Subsequent introduction of fluorine into the ethylene molecule reduces the yield of $C_5H_5NiC_5H_7$. The reaction with tetrafluoroethylene gives rise to a compound with the general formula $C_{10}H_{10}NiC_2F_4$, [56] to which structure (XIII) was attributed[56, 57]:



(XIII)

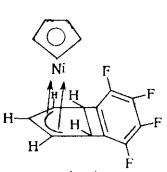


(XIV)

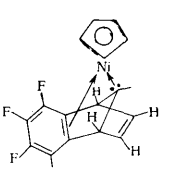
When the dimethyl ester of acetylenedicarboxylic acid is employed as the dienophile, its electron-withdrawing groups favour the addition of the ester via a Diels – Alder reaction, which results in a 68% yield of [2, 3-bis-methoxycarbonyl)-2 π, 5-norbornadien-7-yl](π-cyclopentadienyl) nickel (II) (XIV)[58].

Its structure was confirmed by X-ray diffraction analysis[59]. ^{1}H NMR spectra are also satisfactorily consistent with the proposed structure. Apart from the singlets due to the protons in the cyclopentadienyl ring and the methoxycarbonyl group, the spectrum of (XIV) contains three groups of signals two of which have equal intensities and the third has an intensity smaller by a factor of two. This last signal is in the region of the highest field, which can be accounted for have an effect of the anisotropy of the central metal atom (nickel) on the single proton of the 7-C carbon atom of the norbornadiene ligand[57, 59]. The ^{1}H NMR spectrum of compound (XIII) also has three groups of signals with intensity ratios of 2 : 2 : 1, but the signal with the lowest intensity is observed in the region of the lowest field. This is evidence for the presence of a π-allyl system in the molecule[40, 57, 60]. All these hypotheses have not so far been confirmed by X-ray diffraction studies.

When nickelocene was allowed to react with tetrafluorodehydrobenzene[61], different amounts of both structural isomers with the general formula $(C_5H_5)_2NiC_6F_4$ were isolated:



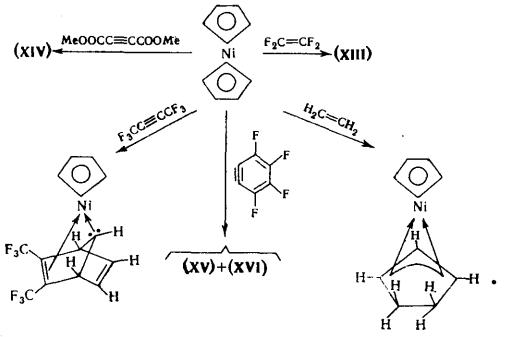
(XV)



(XVI)

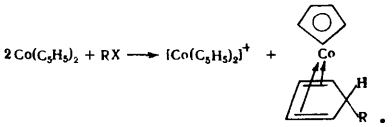
Thus the cyclopentadienyl ligand can combine with olefinic and acetylenic derivatives having electron-accepting groups

in the 1, 2- and 1, 4-positions. This results in the formation of a π-allyl or pseudobutadiene system: §



The addition of olefins, alkyl halides, polyhalogenoalkanes, acyl halides, α-halogenoketones, etc, to cobaltocene takes place with retention of the diene system of the cyclopentadiene fragment. Cobaltocene reacts with tetrafluoroethylene[62]. The infrared spectrum of the products contains ν_{C-H} bands at 3085 and 2940 cm^{-1}. The ^1H NMR spectrum of the compound shows four signals with intensity ratios of 5 : 2 : 2 : 1. On the basis of a detailed analysis of these data[63], the authors concluded that the compounds formed have the structure $C_5H_5CoC_5H_5(CF_2)_2C_5H_5CoC_5H_5$.

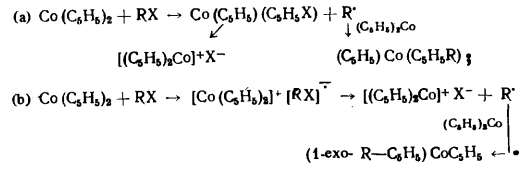
The reaction of cobaltocene and the cobalticenium cation with different organohalogen compounds takes place similarly[43, 64]:



(XVII)

The products have the structure (XVII), where R = CH_2Cl, CH_2Br, $CHCl_2$, $CHBr_2$,[65] etc.[55]. The interaction of cobaltocene with allyl, benzyl, and propargyl halides (R = = $C_6H_5CH=CHCH_2$, $C_6H_5CH_2$, and $C_6H_5C\equiv CCH_2$) was also investigated[66]. Benzoyl chloride[28], α-halogenoketones, and α-halogeno-esters react similarly[65, 67]. Cobaltocene dissolves in chloroform and chlorobenzene without change[65]. However, when the reaction is carried out in the presence of oxygen, a high yield of a compound (XVII), where R = = CCl_3, is formed[68]. Under these conditions, cobaltocene also reacts with acetonitrile, propionitrile, phenylacetylene, and acetone[68], forming the corresponding compounds (XVII). The reaction with acetone gives rise to the dinuclear complex $(C_5H_5CoC_5H_5CH_2)_2CO$.[68]

Two alternative mechanisms of the reaction between cobaltocene and organohalogen compounds have been considered[65, 66, 69]:



§ Nickelocene reacts with perfluorobutyne not only by an addition mechanism but also via a ligand exchange mechanism. A small amount of $(C_5H_5Ni)_2(C_4F_6)$ was isolated[56].

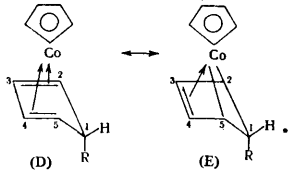
A kinetic study of the reaction did not permit an unambiguous choice. However, the authors are inclined to favour the second mechanism[69] in view of the following qualitative findings: firstly, the rate of reaction of benzyl bromide derivatives is much higher for electron-accepting substituents (p-CN, p-COOEt) and, secondly BBr_3 is known to react with cobaltocene at a temperature as low as -80°C, while $(CH_3)_3NBBr_3$ does not react at 60°C. BBr_3 has more pronounced electron-accepting properties and a higher B – Br bond energy than $(CH_3)_3NBBr_3$. Evidently the reactivity is determined by the electron-accepting properties and not the dissociation energy of the B – Br bond. This conclusion is confirmed also by the finding that the reactivity of $CHBr_3$ in relation to cobaltocene is much lower than that of boron bromide, while the energy of the C – Br bond is also significantly lower than that of the B – Br bond [D(B – Br) = 87.4 kcal $mole^{-1}$; D(C – Br) = 55.5 kcal $mole^{-1}$][69].

The data for the decomposition of azoisobutyronitrile in the presence of cobaltocene are consistent with the proposed radical reaction mechanism[70]. The product is compound (XVII), where R = $C(CH_3)_2CN$. On the other hand, the reaction of chlorotriphenylmethane with cobaltocene results only in the oxidation of the latter to cobalticenium ions[71]. It was suggested that the reaction proceeds according to the equation:

$$(C_5H_5)_2Co + Ph_3C^+ \rightarrow [(C_5H_5)_2Co]^+ + [Ph_3C^\cdot].$$

It is believed[71] that the reaction of nickelocene with the carbonium ion also results in the formation of the nickelicenium cation. However, the low stability of this compound and its paramagnetic properties give rise to the possibility of further interaction between $[(C_5H_5)_2Ni]^+$ and the $(C_6H_5)_3C\cdot$ radical with formation of the complex. $C_5H_5NiC_5H_5C(C_6H_5)_3$. By virtue of its instability, the latter decomposes into $NiCl_2$ and $C_5H_5-C(C_6H_5)_3$.[71]

The study of *exo*-phenylcyclopentadienecyclopentadienylcobalt[53] showed that the $C_{(1)}$ carbon atom deviates from the plane of the cyclopentadiene ligand by 36° and the bond lengths in the "butadiene" fragment are non-uniform (the $C_{(3)}-C_{(4)}$ distance is a minimum, amounting to 1.38 Å):



(D) (E)

Therefore it was suggested that the carbon atoms in the 2- and 5-positions be regarded as sp^3-hybridised, which would imply that the complex is predominantly in form (F). However, X-ray diffraction study of *exo*-benzoylcyclopentadienecyclopentadienylcobalt showed that the bond order in the "butadiene" system of cyclopentadiene is relatively constant[53]. The authors are inclined to attribute these contradictions to differences between the inductive effects of the benzoyl and phenyl substituents.

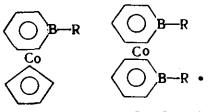
The bond between the substituent and the cyclopentadiene fragment of an *exo*-substituted organocobalt compound is known to be fairly labile. *Exo*-(trichloromethyl)cyclopentadiene(cyclopentadienyl)cobalt splits off a CCl_3 group and is converted into the cobalticenium cation on acid hydrolysis or on standing in acetone. $C_5H_5CoC_5H_5CCl_2COOCH_3$ behaves similarly[67]. On the other hand, although chlorine exchange between LiCl and $(exo\text{-}CCl_3-C_5H_5)Co(C_5H_5)$ is not observed, the C – X bond in compounds of the type $(exo\text{-}XCH_2-C_5H_5)Co(C_5H_5)$[55, 72, 73] or the B – X bond in the

compound (*exo*-$C_6H_5BXC_5H_5$)CoC_5H_5 (Herberich et al.[74]) is thermally unstable and undergoes heterolysis extremely readily.

Thus whereas $(C_5H_5)Co(C_5H_5CF_2CF_2C_5H_5)Co(C_5H_5)$ sublimes *in vacuo* at 125°C and $C_5H_5CoC_5H_5 - CHCl_2$ and $C_5H_5CoC_5H_5 - CH_2Cl$ are still stable at 70°C, the bromo-compounds decompose appreciably already at room temperature and $C_5H_5CoC_5H_5CH_2I$ decomposes in the solid state at 0°C. The heterolysis of the C – X bond in these compounds terminates in a ring expansion reaction and the formation of cyclohexadienylcyclopentadienylcobalt halide. The reaction with the pseudocarbonium ions derived from organocobalt compounds leads to the formation of a new class of paramagnetic cobalt complexes[75]. The unsubstituted borabenzene

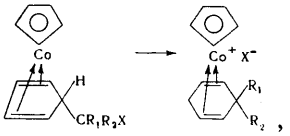


is unknown. However, the reaction of cobaltocene with substituted boron dibromide and subsequent heterolysis of the C – B bond in the resulting compound [*exo*-Br(R)BC_5H_5] CoC_5H_5 and then the formation of a six-membered ring leads to cobalt complexes of substituted borabenzene ¶ [74, 75]:



The compounds have one unpaired electron, the magnetic moment of which is 1.8 ± 0.1 Bohr magnetons[75]. The ionisation potentials of these compounds are higher than that of cobaltocene, which indicates more pronounced electron-accepting properties of the group C_5H_5BR compared with C_5H_5.

The reaction of the pseudocarbonium cation,



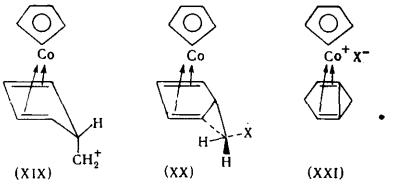
(XVIII)

discovered by Herberich and coworkers[55, 65, 72] resembles the solvolysis of alkyl halides.

Compounds (XVIII) react under very mild solvolytic conditions[72], such that their structural analogues isobutyl and neopentyl halides hardly ionise. The rate of reaction depends on the medium and the positions of the substituents in the cyclopentadiene ligand (*endo*- and *exo*).

In non-polar solvents, the rate is insignificant, while in acetone, methanol, or their mixture with water the reaction proceeds smoothly and virtually without side products. The reactivity of compounds (XVIII) decreases in the series I > Br > Cl. The effect of substituents on the rate of reaction is the same as for the solvolysis of alkyl halides which has an S_N1 mechanism. Thus the bromo-derivative (XVIII), where $R_1 = R_2 = CH_3$, is much more labile than the secondary bromo-substituted derivative (XVIII), where $R_1 = CH_3$ and $R_2 = H$. Moreover, this reaction is observed only when the substituent occupies the *exo*-position[77].

Thus the authors believe that the order of the reaction (S_N1), the solvolytic effect, which is somewhat weaker than in the solvolysis of t-butyl halides[78], and the entropy of activation[72] indicate the heterolysis of the C – X bond in compounds (XVIII) as the rate-determining stage of the reaction. It is noteworthy that the reaction of primary alkyl chlorides (XVIII) ($R_1 = R_2 = H$, X = Cl) in methanol is faster than the solvolysis of t-butyl chloride[79]. This enhanced reactivity of primary alkyl halides is believed[72] to be evidence in support of the stabilisation of the intermediate ion (XIX) by the entire electron system of the $C_5H_5CoC_5H_5$ group. It is suggested that two processes take place synchronously — heterolysis of the C – X bond and rearrangement of the cyclopentadiene ligand. The authors believe [72] that the six-membered ring is formed either via the complex (XX) or via a short-lived intermediate (XXI):

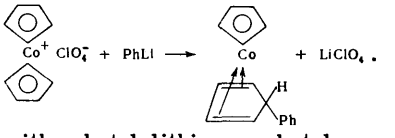


(XIX) (XX) (XXI)

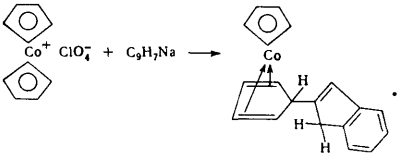
The kinetic study of the process is consistent with either of the two mechanisms proposed.

3. Reactions with Nucleophilic Agents

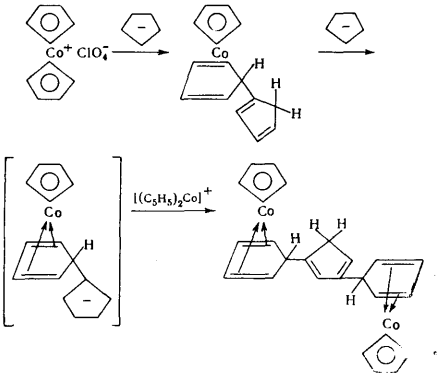
Reactions involving nucleophilic addition to the cyclopentadienyl ligand of nickelocene, where organometallic compounds are employed as the attacking agents, are so far unknown. The cobalticenium cation readily reacts with organolithium or organomagnesium compounds[28] and also with sodium hydroxide and sodamide[80]:



The reaction with n-butyl-lithium, n-butylmagnesium bromide, and methylmagnesium iodide takes place similarly. The reaction of cobalticenium perchlorate with indenylsodium also gives rise to a "normal" addition product — indenylcyclopentadienecyclopentadienylcobalt[81]:



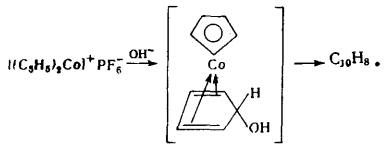
Sodium cyclopentadienide and its methyl derivative react with cobalticenium salts to form dinuclear complexes[81]. The suggested reaction mechanism can be represented as follows in a general form:



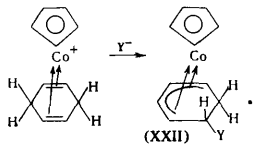
¶ 1, 1'Bis(methoxyborabenzene)cobalt has been investigated by X:ray diffraction[76].

The central ring may be hydrogenated. Initially two hydrogen atoms are added readily and then a further two but with greater difficulty. The compound does not react with maleic anhydride, probably owing to steric factors[81].

The reaction between the cobalticenium cation and sodium hydroxide with formation of azulene has been carried out[80]. The authors believe that it proceeds via the following mechanisum:



Nucleophilic agents such as sodium borohydride[72], ammonia, aliphatic amines, and sodium methoxide[82] add readily to the cyclohexadienyl ligand of the cyclohexadienylcyclopentadienylcobalt cation; the product is cyclopentadienylcyclohexa-1, 3-dienecobalt (XXII):



(XXII)

There is an analogous reaction of the cyclohexadienyltricarbonyliron cation[83, 84].

Thus the numerous addition reactions characteristic of cobaltocene and nickelocene distinguish these compounds from ferrocene. The ferrocene system, like the benzene system, is extremely passive in relation to reactions involving the addition of hydrogen, alkyl halides, alkenes, alkynes, and other reagents[1, 2].

V. LIGAND EXCHANGE REACTIONS IN COBALTOCENE AND NICKELOCENE

The ligand exchange reaction is characteristic of all three types of sandwich compounds discussed in the present review. However, the nature of the ligand capable of replacing the cyclopentadienyl group in ferrocene, nickelocene, and cobaltocene is different. In the first case the ligands can be benzene[85-87], cyclopentadiene[88], their substituted derivatives, and many others. The ligand exchange reaction has been investigated most extensively in nickelocene. The cobalticenium system is more passive in ligand exchange processes.

The reaction of cobaltocene with $Fe(CO)_5$ gives rise to dicobalticenium tridecacarbonylferrate[89]. Under analogous conditions, nickelocene enters into a ligand exchange reaction and is converted into (cyclopentadienyliron)cyclopentadienylnickel tricarbonyl[90, 91]. This is not fortuitous either. Whereas ligand exchange reactions are extremely characteristic of nickelocene and many experimental data have been accumulated in this field, under these conditions cobaltocene is usually converted into a cation or undergoes no change whatever. Similarly, when a triphenylphosphonium halide is allowed to react with nickelocene, the phosphine ligand is coordinated to the nickel atom and a cyclopentadienyl fragment is split off[92], while cobaltocene is oxidised with formation of cobalticenium halide[93]. Mass-spectrometric studies on the dicyclopentadienyl compounds of cobalt and nickel[94, 95] have shown that the energy required to form metallocenium ion $[(C_5H_5)_2M]^+$ is much lower for cobaltocene than for nickelocene (6.21 eV and 7.16 eV † respectively). The stability of the cobalt–cyclopentadienyl linkage in the cobalticenium cation is well known[11, 24-27]. Moreover, the formation of the $[C_5H_5M]^+$ fragment takes place more readily in the case of nickelocene. The energies of ionisation of cobaltocene and nickelocene, resulting in the formation of $[C_5H_5M]^+$, are 14.00 and 12.59 eV respectively. Probably this can explain the finding that nickelocene reacts readily with various nucleophilic agents under mild conditions, exchanging one or two cyclopentadienyl rings. Thus, whereas nickelocene reacts with PF_3 at 60°C and normal pressure to form tetrakis(trifluorophosphine)nickel[98], the complex $(C_5H_5)Co(PF_3)_2$ was obtained from cobaltocene and PF_3 at 170°C and a pressure of 300 atm.[99]. Under analogous conditions, cobaltocene and its derivatives react with carbon monoxide, which results in the isolation of the extremely labile cyclopentadienylcobalt dicarbonyl[20, 100]:

$$(RC_5H_4)_2Co \xrightarrow{CO} RC_5H_4Co(CO)_2.$$

[R = H (Fischer and Jira (Ref.100) or $COOCH_3$ (Rosenblum et. al. (Ref.20)]

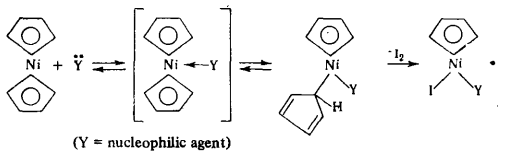
1. SUBSTITUTION OF BOTH CYCLOPENTADIENYL LIGANDS

The capacity of nickelocene to exchange readily a cyclopentadienyl ligand resulted in the formation under mild conditions of various nickel complexes. The analogous reaction with $Ni(CO)_4$ or nickel halides takes place under more severe conditions. Various phosphorus- and nitrogen-containing nickel complexes were obtained in this way[101-103]. The substitution of both cyclopentadienyl ligands in the cobaltocene molecule take place under more severe conditions (on refluxing in dioxan for a week)[104]. The product is formed in low yield:

$$(C_5H_5)_2Co + P(OPh)_3 \rightarrow (Co[P(OPh)_3]_4)_n.$$

2. SUBSTITUTION OF ONE CYCLOPENTADIENYL LIGAND

When equimolar amounts of nickelocene and triphenylphosphine react in benzene at 50°C, one cyclopentadienyl ring is substituted. Further treatment with iodine or hydrogen chloride leads to the formation of $(C_5H_5)Ni(R_3P)X$, where X = Cl or I.[105]. It is believed[105] that the nucleophilic agent is initially coordinated to the nickel atom. Simultaneously with or after the coordination, a $\pi-\sigma$ rearrangement of one of the cyclopentadienyl rings takes place. The final stage of the process involves the stabilization of the unstable σ complex by the substitution of the σ-linked cyclopentadienyl ligand:

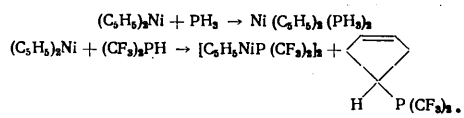


(Y = nucleophilic agent)

The results obtained in the study of the kinetics of the reaction of nickelocene with mercaptans are consistent with the mechanism proposed[106]. Reactions of nickelocene

† The ionisation potential quoted is consistent with other published values: 6,8 eV,[96] 7.06 eV,[94] and 6.75 eV.[97]

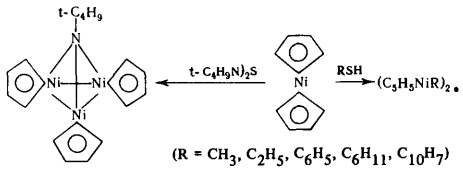
with phosphine[107] and bis(trifluoromethyl)phosphine are known[108]:



In both cases the ease with which the phosphine forms a cluster or interacts with unsaturated hydrocarbons is striking. It is interesting that the reaction between an olefin and a phosphine takes place only following irradiation with ultraviolet light[108]. Therefore it has been suggested [108] that the nickel atom behaves at a catalyst in the addition of a phosphine to the cyclopentadienyl ligand. On heating a 4 – 6-fold excess of $P(OR)_3$ (R = C_6H_5, CH_3, or C_2H_5) with cobaltocene for 3 – 7 days at 100°C, one cyclopentadienyl ligand is also exchanged[104]. The stability of the product $C_5H_5CoL_2$ depends on the nature of the substituent in the ligand L. Analysis of the complexes known so far makes it possible to arrange these compounds in the following series in terms of the decrease of their resistance to the action of oxidising agents: L = $P(OC_6H_5)_3$ > > $PF_3 \simeq P(OCH_3)_3 \simeq P(OC_2H_5)_3 > CO > P(C_6H_5)_3$.[104]

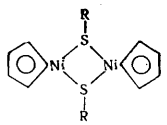
a. Reactions Yielding Polynuclear Complexes

Reactions of nickelocene and 1, 1′-dimethylnickelocene with thioalcohols[106, 109, 110] and the di-imide of sulphurous acid[111] are known. They result in the formation of organonickel compounds containing sulphur[109, 110] or nitrogen[111] bridge atoms:



(R = CH_3, C_2H_5, C_6H_5, C_6H_{11}, $C_{10}H_7$)

The reactions have been carried out with equimolar amounts of the initial compounds in benzene at room temperature. The dark-brown compounds are diamagnetic and stable in air. It has been suggested[109] that the sulphur atoms are sp^3-hybridised and the compounds have the following structure:

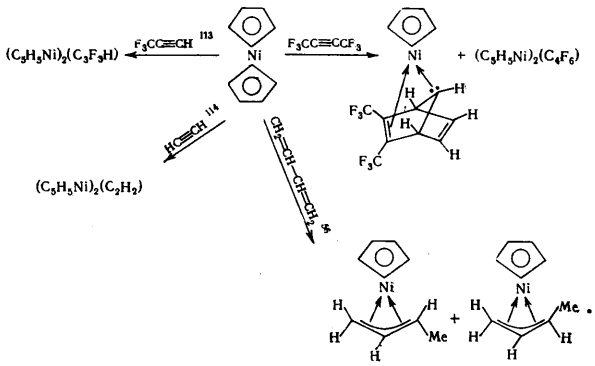


In a study of the polymerisation of cyclohexyl isocyanide in the presence of catalytic amounts of nickelocene, the compound $(C_5H_5NiCNC_6H_{11})_2$ was isolated[112]. $(C_5H_5NiCO)_2$ and $(C_5H_5Ni)_2C_2H_2$ were also used as catalysts. It was shown that nickelocene is the most effective catalyst of the process[112].

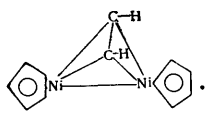
b. Reactions with Unsaturated Compounds

Earlier it was noted that, depending on the electron-accepting properties of the substituents at the unsaturated carbon atom, the reactions of nickelocene with unsaturated hydrocarbons involve addition to the 1, 2- or 1, 4-positions. As the triple bond becomes more nucleophilic, the ligand exchange becomes the dominant process in the reactions of nickelocene with unsaturated compounds.

Thus, whereas the reaction of nickelocene with perfluorobut-2-yne[56] leads to a mixture of products of addition to the 1, 4-positions and of ligand exchange, the reaction with trifluoropropyne[113] results in the formation of a green complex the elemental analysis and mass spectra of which correspond to the formula $(C_5H_5Ni)_2(C_3F_3H)$. A compound of a similar type was obtained from nickelocene and acetylene[114]:



X-ray diffraction analysis of $(C_5H_5Ni)_2(C_2H_2)$ showed[115] that acetylene occupies a bridging position between two nickel atoms:

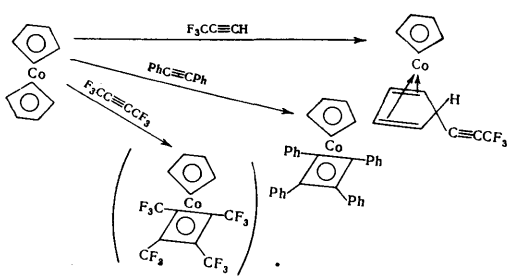


It is noteworthy that cobaltocene can also react with trifluoropropyne[113], but this leads to the formation of a compound with the general formula $(C_5H_5)Co(C_5H_5C \equiv CCF_3)$. ^1H and ^{19}F NMR spectra showed that this is a product of the "normal" addition to the cobaltocene molecule[113]. The reaction of perfluorobut-2-yne with cobaltocene results in the formation of traces of the stable complex $(C_5H_5)CoC_8F_{12}$,[116] and the reaction with tolane terminates with formation of a high yield of the aromatic complex $(C_5H_5)Co[C_4(C_6H_5)_4]$[116] (see scheme on p. 286). The complexes $(C_5H_5)Co(C_4R_4)$, where R = $Si(CH_3)_3$, CoCh3, etc, can be obtained similarly[145].

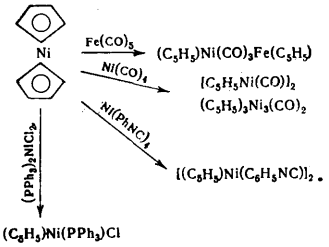
c. Disproportionation Reactions

The ease with which nickelocene exchanges its cyclopentadienyl rings promotes its involvement in disproportionation reactions. Reactions with $Fe(CO)_5$,[90, 91] $Ni(CO)_4$,[117–120] $Ni(C_6H_5NC)_4$,[121] and $[(C_6H_5)_3P]_2NiCl_2$[121, 122] are known.

Schematic representation of the interactions of cobaltocene with unsaturated compounds.



The disproportionation and synproportionation reactions of ferrocene homologues take place in the presence of aluminium chloride[88]:

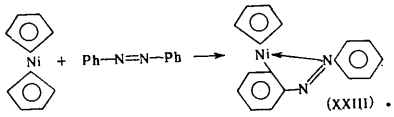


The only disproportionation reaction of cobaltocene known hitherto is the reaction with cyclobutadienyltetraphenylpalladium dibromide[123]:

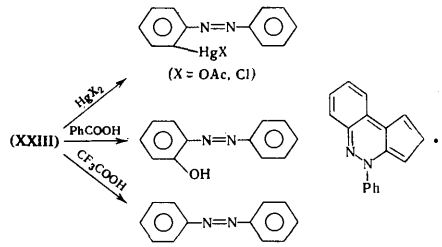
$$(C_5H_5)_2Co + (C_4Ph_4)\,PdBr_2 \rightarrow (C_5H_5)\,Co\,(C_4Ph_4).$$

d. Reactions Involving the Formation of Complexes with an M – C σ Bond.

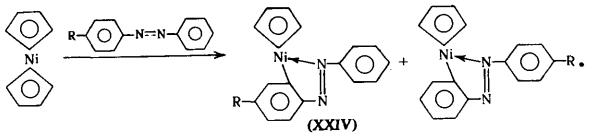
The reaction of nickelocene with azobenzene was described for the first time by Kleiman and Dubek[124]:



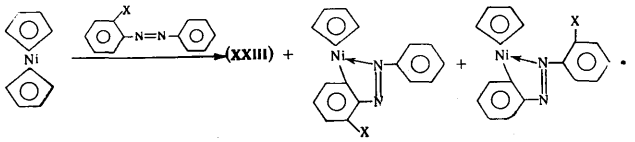
The study of the reactions and the ^1H NMR spectra of (2-azophenyl)phenylcyclopentadienylnickel (XXIII) demonstrated the existence of an Ni – C σ bond with the *ortho*-carbon atom of one of the benzene rings[125]:



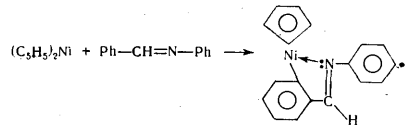
Examination of the influence of various *ortho*- and *para*-substituents in azobenzene on the nature of the compounds formed in the reaction[126] showed that *para*-substituted azobenzenes [$(CH_3)_2N$, CH_3O, CH_3, F, Cl, $COOCH_3$, CN, or NO_2] react with nickelocene to form the complexes (XXIV):



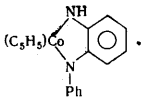
The reaction of ortho-substituted halogenoazobenzenes with nickelocene takes place anomalously:



The rate of formation of compounds (XXIII) increases in the series azobenzene < *o*-chloroazobenzene < *o*-bromoazobenzene. Benzylideneaniline reacts with nickelocene like azobenzene[127]:



Cobaltocene also reacts with azobenzene[128]. However, here the product is a complex to which the following structure has been assigned:



The yield of the reaction is 2.4%.

When nickelocene is treated with an alky- or alkynylmagnesium iodide in the presence of triphenylphosphine[129], nickel complexes also containing an Ni – C σ bond are formed:

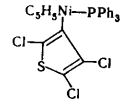
$$(C_5H_5)_2Ni + Ph_3P \xrightarrow{RMgI} C_5H_5Ni\,(Ph_3P)\,\sigma\text{-}R.$$
$$(R‡=Me \quad or \quad C\equiv CR').$$

Another convenient procedure for the preparation of these compounds involves the reaction between $(C_5H_5)Ni[(C_6H_5)_3P]Cl$ and various organolithium or organomagnesium compounds[122, 131, 132]:

$$C_5H_5Ni\,(Ph_3P)\,Cl + RMgX \rightarrow C_5H_5Ni\,(Ph_3P)\,\sigma\text{-}R,$$

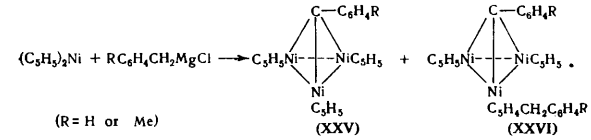
where R = aliphatic and aromatic substituents.

The above organonickel compounds consist of dark-green diamagnetic crystals which are fairly stable in air. The stability of complexes of the type $(PR_3)_2NiR'_2$ or $(PR_3)_2NiR'X$ is known to increase in the following sequence depending on the nature of the substituent: alkyl < ethynyl or substituted ethynyl ≃ *o*-aryl[133]. This sequence is probably determined by the possibility of the formation of a $d_\pi - p_\pi$ bond between the nickel atom and σ - R and also by the inhibition of the rotation of the *ortho*-substituted phenyl group about the Ni – C bond, which likewise promotes the interaction of the ligand π orbitals with the *d* orbitals of the nickel atom[133]. In this connection, it is interesting to note that, in contrast to the stable complex



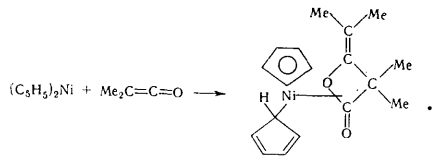
a thiophen derivative without chlorine atoms has not been isolated at all[132].

‡ On the other hand, the reaction of nickelocene with benzylmagnesium chloride at room temperature results in the formation of nickel cluster compounds[130]:



It is suggested[130] that compound (XXVI) is formed owing to an unusual alkylation process: (XXVI) + $RC_6H_4CH_2MgCl$ → (XXVI), which has been confirmed experimentally.

The interaction of a ketone with nickelocene[134] gives rise to a compound in which one of the cyclopentadienyl ligands is linked to the nickel atom via a σ bond:



VI. ELECTRON-DONATING PROPERTIES OF COBALTOCENE AND NICKELOCENE

Analysis of the chemical reactions of cobaltocene and nickelocene reveals significant differences between the chemical behaviour of each compound. This is a consequence of the electronic structures of these π complexes. Moreover, the different stabilities of their cations, $[(C_5H_5)_2CO]^+ > [(C_5H_5)_2Ni]^+$ and $[(C_5H_5)_2Ni]^{2+}$, play a significant role.

1. CONDITIONS GOVERNING THE FORMATION OF THE METALLOCENIUM CATION.

The oxidation-reduction potentials of the metallocenes (Fe, Co, Ni) were determined initially in 90% ethanol using 0.1 M sodium perchlorate solution as the electrolyte. The results were $E_{1/2}$ = +0.30 V for ferrocene, $E_{1/2}$ = = -1.16 V for cobaltocene[135], and $E_{1/2}$ = -0.08 V for nickelocene[136]. Further studies in this field led to a revision of these values[42, 45].

The polarographic reduction of substituted cobalticenium salts at a mercury electrode in an aqueous alcoholic medium was also investigated[32]. The half-wave potentials $E_{1/2}$ are independent of the pH of the medium. The effect of substituents on $E_{1/2}$ is of the usual type[32]. Table 2 lists for comparison the oxidation-reduction potentials of the unsubstituted metallocenes and certain π acceptors.

Table 2. Oxidation-reduction potentials of the metallocenes (Fe, Co, Ni) and certain π aceptors*.

Donor	$E°$, V	Refs.	π Acceptor	$E°$, V	References
$(C_5H_5)_2$ Fe	+0.30	137	*p*-benzoquinone	−0.50	138
	+0.42	42	*p*-chloranil (CA)	+0.01	138
			tetracyanoethylene (TCE)	+0.15	139
$(C_5H_5)_2$ Co	−0.98	42			
$(C_5H_5)_2$ Ni	+0.01	42	2,3-dichloro-5,6-dicyanoquinone (DDQ)	+0.51	138

* All the E values were determined in acetonitrile.

The metallocenes exhibit a high electron-donating capacity, which is reflected in their tendency to form readily salts and charge-transfer complexes.

Interaction with Strong Oxidising Agents (Halogens, Thiocyanogen, and Picric Acid)

The electron deficiency of the π acceptor and the electron-donating properties of the metallocene determine the type of the charge-transfer complex formed. Partial charge separation between the components, $(\text{Don.})^{+\delta}$ $(\text{Acc.})^{-\delta}$, leads to the formation of a π complex of the dative type[140]. In this case the infrared and ultraviolet spectra of the π complex exhibit all the features characteristic of the metallocene and the π acceptor. When the charge separation is more complete, a charge-transfer complex of the ionic type is produced[141]. Further development of this process terminates with the formation of a salt in which the metallocene is converted into the metallocenium cation and the π acceptor behaves as the anion. Treatment of ferrocene with chlorine[142] or bromine[143] is known to result in the formation of a ferricenium halogenoferrate (III) salt $[(C_5H_5)_2Fe]FeX_4$. Thiocyanogen, the oxidising capacity of which is intermediate between those of bromine and iodine, forms the salt $[(C_5H_5)_2Fe]_2Fe(NCS)_4$, but in this case the metal in the anion is in a lower state of oxidation[144]. The series is terminated by iodine[146, 147], which forms polyiodides with ferrocene. When thiocyanogen is allowed to react with cobaltocene, the latter does not decompose like ferrocene. The product is cobalticenium thiocyanate $[(C_5H_5)_2Co](NCS)$.[144]

Iodine reacts similarly with cobaltocene[148], forming cobalticenium tri- or octo-iodide. When iodine reacts with nickelocene, the latter is decomposed[148]. According to its chemical properties, bis(tricarbonylcyclopentadienylchromium) is an analogue of iodine. Its reaction with cobaltocene gives rise to the cobalticenium salt $[(C_5H_5)_2Co][C_5H_5Cr(CO)_3]$.[149] Treatment of cobaltocene with HX (X = Cl, Br, or I) in ether results in the formation of cobalticenium tetrahalogenocobaltates $[(C_5H_5)_2Co]_2CoX_4$.[93] The authors believe[93] that the reaction proceeds in several stages:

$$(C_5H_5)_2Co^{\cdot} + HX \rightarrow [(C_5H_5)_2Co]^+X^- + H^{\cdot}, \quad (1)$$

$$[(C_5H_5)_2Co]^+X^- + HX \xrightarrow{\text{slow}} C_5H_6 + C_5H_5^{\cdot} + CoX_2^{\cdot}, \quad (2)$$

$$2[(C_5H_5)_2Co]^+X^- + CoX_2 \xrightarrow{\text{rapid}} [(C_5H_5)_2Co]_2^+[CoX_4]^-. \quad (3)$$

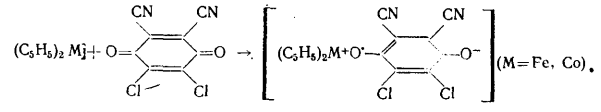
Hydrogen fluoride, being a weak acid, cannot decompose the cobalticenium ion [Eqn. (2)] and therefore the reaction results in the formation of the complex $[(C_5H_5)_2Co]HF_2$.[93] The reaction of the hydrogen halides HX (X = Cl, Br, or I) in the presence of triphenylphosphine with cobaltocene in ethereal solution leads to the formation of $[(C_5H_5)_2Co]^+X^-$ (X = Cl, Br, or I) as the main product and as well as small amounts of $[(C_5H_5)_2Co]_2^+[CoX_4]^-$ and $[(C_5H_5)_2Co][Co(PRh_3)X_3]$.[150, 151] Trichloroacetic acid reacts with ferrocene to form a paramagnetic compound with reducing properties[152]. The authors believe that an electron of the ferrocene molecule is bound by the acid proton, as happens in the reaction between an alkali metal and ammonia or an amine[153]. The interaction between trichloroacetic acid and cobaltocene takes place similarly. The product is the paramagnetic compound $[(C_5H_5)_2Co]^+(BH^-)(BH)_2$, where B = CCl_3COO.[154] However, the usual cobalticenium salt is also formed in this case together with the charge-transfer complex, which is fully consistent with the electron-accepting properties of cobaltocene.

Picric acid reacts with ferrocene to form a charge-transfer complex[155, 156], while its reactions with cobaltocene[148] and nickelocene[148] give rise to salts §.

§ However, it has been shown that in the reaction between picric acid and cobaltocene, a charge-transfer complex is formed together with the cobalticenium salt[154].

2. CHARGE-TRANSFER COMPLEXES

Treatment of ferrocene[157] or cobaltocene[157,158] with 2, 3-dichloro-5, 6-dicyanoquinone (DDQ) or 7, 7, 8, 8-tetracyanoquinodimethan results in both cases in the formation of stable complexes with a 1 : 1 component ratio. The infrared spectra of the complexes with DDQ do not contain the ν_{CO} band (1680 cm^{-1}), but a new band appears at 1590 cm^{-1}, which has been assigned to the vibrations of the phenoxy-group[159]; this suggests that these compounds are ionic π complexes[157]:



It is noteworthy that only the addition of a solution containing a 40-fold molar excess of $AgClO_4$ relative to the DDQ – cobaltocene and DDQ – ferrocene complexes results in the appearance in the ultraviolet spectra of these compounds of the band which has been assigned to absorption by the metallocenium cations. It has been shown experimentally[157] that the component ratio in the DDQ – nickelocene complex is not 1 : 1 and the infrared spectrum of this compound differs significantly from those of the corresponding ferrocene and cobaltocene π complexes. It is most probable that, by virtue of its electron-donating properties, nickelocene forms a mixture of salts of the singly and doubly-charged cations, $[(C_5H_5)_2Ni]^+$ and $[(C_5H_5)_2Ni]^{2+}$, in its reaction with DDQ.

Tetracyanoethylene (TCE)[157] and *p*-chloranil (CA)[160] form charge-transfer complexes with cobaltocene and nickelocene, which differ significantly in stability. As a stronger electron acceptor, TCE forms unstable compounds with cobaltocene and nickelocene, which can be kept in an atmosphere of nitrogen or at a low temperature (-80°C). The interaction with CA, which is a weaker electron-acceptor than TCE, leads to the formation of stable complexes. This anomaly can probably be accounted for by the lower "electron capacity" of the tetracyanoethylene system compared with the CA aromatic molecule and also by the higher electron-donating capacity of cobaltocene and nickelocene compared with ferrocene. This explanation has been confirmed by the properties of the TCE–ferrocene[161] and TCE – bis(tetrahydroindenyl)iron[157] complexes. The introduction of an alkyl substituent is known to enhance the electron-donating properties of the ferrocene system, increasing thereby the likelihood of the transfer of electron density to the π acceptor. Presumably the π complex of substituted ferrocene with TCE is less stable than the complex with an aromatic π acceptor. Indeed the TCE–bis(tetrahydroindenyl)iron complex is labile, while the complex with DDQ is quite stable[157]. On the basis of ultraviolet and infrared spectroscopic data, the TCE–ferrocene complex was assigned to the dative type[157,161-163] and the TCE–cobaltocene complex was assumed to be ionic[157], CA, the electron-accepting properties of which differ only slightly from those of TCE, forms similar complexes with ferrocene[157], cobaltocene[157,164], and nickelocene[157,160].

The data presented show that, depending on the relative contributions by the electron-donating and electron-accepting properties of both components of the charge-transfer complexes, the degree of charge separation between the components may be various. Dative complexes are usually formed by ferrocene. The interaction with cobaltocene and nickelocene leads to the formation of ionic complexes.

The capacity to form complexes with electron acceptors is a general property of the three types of compounds considered.

* * *

In conclusion we shall consider the properties of the metallocenes which must be taken into account in their synthesis. The metallocenes can be obtained in the gas phase[165,166] by the reaction between metal salts and cyclopentadiene. However, the yield is not always quantitative. Cyclopentadiene or its dimer are used as the starting materials for the synthesis of the metallocenes by reaction with the corresponding metal carbonyls[136,167]:

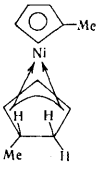
$$C_5H_6 + M_n(CO)_m \rightarrow (C_5H_5)_2M + CO$$

for M=Fe, m=5, n=1; for M=Co, m=8, n=2).

The main product of this type of reaction with nickel carbonyl is cyclopentadienylcyclopentenylnickel. Nickelocene is formed as a side product in an amount not exceeding 5%[136,168,169]:

$$C_5H_6 + Ni(CO)_4 \rightarrow C_5H_5NiC_5H_7 + (C_5H_5)_2Ni.$$

The interaction of $CH_3C_5H_5$ with $Ni(CO)_4$ led to the isolation of a red diamagnetic compound to which the following structure was attributed on the basis of ^1H NMR spectra[170]:



When cyclopentadiene is introduced into the reaction in the form of the anion, the dimer of cyclopentadienylnickel carbonyl $(C_5H_5NiCO)_2$ is isolated[171]:

$$C_5H_5Na + Ni(CO)_4 \rightarrow (C_5H_5NiCO)_2.$$

Probably this compound is obtained by a ligand exchange reaction between the nickel carbonyl and the nickelocene formed, which is extremely typical for the chemistry of the latter[117-120]. It is noteworthy that the interaction of di-μ-carbonyldi(cyclopentadienyl)dinickel(0) $(C_5H_5NiCO_2)$ with a monodentate ligand L {L = CO, $(C_6H_5)_3As$, $(C_6H_5)_3P$, $C_2H_5(C_6H_5)_2P$, $[(CH_3)_2N]_3P$, etc.} leads to the formation of a nickelocene in 30 – 70% yield[172-173]:

$$(C_5H_5NiCO)_2 + 2L \rightarrow Ni(CO)_2L_2 + Ni(C_5H_5)_2.$$

The amount of ionic character of cyclopentadiene or its substituted derivative is also significant in the formation of nickelocene. One can employ different bases, the nucleophilic properties of which are sufficient for the formation of the ionised form of cyclopentadiene. A fairly wide range of amines, with $pK_a < 9$, is usually employed for unsubstituted cyclopentadiene[174]. The so called "amine method" was found to be valid in all three cases. Ferrocene[175,176], cobaltocene[176], its cation[175], and nickelocene[176] were obtained in high yields. More powerful nucleophilic agents can also be used. Among these mention may be made of sodium methoxide[177], potassium hydroxide[178], ethylmagnesium bromide[26,136,179,180], and thallium(I) hydroxide[181-183]. In all these cases, the metallocenes were obtained in high yields. Sodium cyclopentadienide can also be employed as a cyclopentadienylating agent. It is synthesised by metallating cyclopentadiene with metallic sodium[184], sodamide[185,186], sodium hydride[187], or sodium acetylide[188].

It is noteworthy that in the synthesis attention should be concentrated on the choice of the transition metal salt. When nickel chloride is replaced by its acetylacetonate in the reaction with cyclopentadienylmagnesium bromide, the yield of nickelocene increases from 8 to 60%.[136] If cobalt chloride is replaced by the bromide, the reaction of the latter with cyclopentadienylthallium results in a quantitative isolation of the cobalticenium salt instead of the 25% yield in the case of cobalt chloride[181]. On the other hand, the yield of nickelocene increases from 0 to 25 and 70% as nickel(II) chloride is replaced in succession by its bromide[181] and then by hexamminenickel(II) chloride[182]. Cobalticenium salts can be obtained in high yields also by the disproportionation reaction of dihalogenocyclopentadienylcobalt[189]:

$$[C_5H_5CoX_2]_n \rightarrow [C_5H_5)_2Co]^+.X^- + CoX_3,$$

where X = I, Br, or Cl. The π complexes of cobalt can be arranged in the following sequence in terms of the decrease of their resistance to disproportionation: $[Co(C_5H_5)I_2] > [Co(C_5H_5)Br_2] > [Co(C_5H_5)Cl_2]$.[189]

Ferrocene derivatives are usually obtained by an electrophilic substitution reaction[1-10]. The direct introduction of a substituent into cobaltocene and nickelocene molecules is complicated by the ready oxidisability of the compounds and their tendency to undergo addition and ligand exchange reactions. This was discussed above in detail. Therefore cobaltocene and nickelocene derivatives can be obtained either from fulvenes[29, 32, 190] or from substituted cyclopentadienes[33, 191-193, 200] and cyclopentenones[30, 194]. Members of the homologous series of metallocenes [29, 32, 191, 193], polysubstituted heterohomologous series of metallocenes[192, 193], chlorometallocenes[200], homoannular homologues of metallocenes[33, 195], and also hydroxy-derivatives of ferrocene and cobaltocene[30, 194] have been obtained in this way. An interesting method involving the employment of ferrocene derivatives, which are widely available, as the starting materials for the synthesis of other metallocenes, in particular cobalticenium salts, has been described[196]:

$$(RC_5H_4)_2Fe \xrightarrow[2.CoCl_2,\ THF]{1.LiEtNH_2} [(RC_5H_4)Co]^+X^-,$$

(a) R = Et; X = $^1/_2PtCl_6$; (b) THF = Pr; X = $HgCl_3$).

If the substituted cyclopentadiene obtained by the reductive cleavage of ferrocene is isolated as an organothallium derivative, it can be converted into other metallocenes[181, 197, 198]:

$$(R_1R_2C_5H_3)_2Fe \xrightarrow[2.\ TlOH,\ H_2O]{1.\ LiEtNH_2} R_1R_2C_5H_3Tl \xrightarrow{MX_2} (R_1R_2C_5H_3)_2M.$$

(M = Co, Ni).

In addition, nickelocene has been converted into ferrocene[199], which may be important for the identification of nickelocene and its derivatives. Thus interconversions of the dicyclopentadienyl derivatives of the metals in the Fe, Co, Ni triad are possible.

Examination of the chemical behaviour of nickelocene and cobaltocene (substitutions, addition, and ligand exchange reactions) showed that information about the reactions of the first type is comparatively scanty. Therefore in the future the efforts of investigators will probably be directed towards research in this field.

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Institute of Organic Derivatives
of the Elements, USSR Academy
of Sciences, Moscow

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Electrochemical Alkoxylation of Organic Compounds

M.Ya.Fioshin, L.A.Mirkind, and M.Zh.Zhurinov

The review considers current problems of the electrochemical alkoxylation of heterocyclic compounds, unsaturated and aromatic hydrocarbons, carboxylic acids, amines, and ethers. Certain alkoxydimerisation reactions are also discussed. The methods used to carry out alkoxylation reactions are considered. Much attention is given to the present state of studies on the kinetics and mechanism of electrochemical alkoxylation.
The bibliography includes 120 references.

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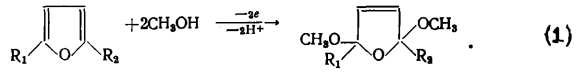
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I. INTRODUCTION

The results of the first experiments on the electrochemical alkoxylation of organic compounds were published at the beginning of the 1950's[1,2]. Over a comparatively short period, numerous studies designed to develop effective electrochemical methods for synthesising a wide variety of alkoxy-derivatives were carried out. Interest in electrolysis as a method for the preparation of compounds of this class is due to the importance of alkoxy-derivatives and also the disadvantages of the chemical methods for their synthesis. Alkoxylated aliphatic and alicyclic organic compounds can be used to synthesise polymers and plasticisers[3-5], valuable lubricating oils[6], emulsifying agents[7], perfumes[8], extractants[9], inhibitors of the oxidation of petroleum products[7], and biologically active preparations[6,10-13].

II. ELECTROCHEMICAL ALKOXYLATION OF HETEROCYCLIC COMPOUNDS

The electrochemical alkoxylation, mainly methoxylation, of furan and its derivatives has been investigated in greatest detail:



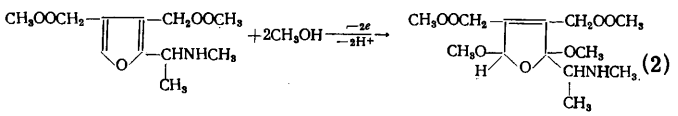
(1)

The electrolysis of a methanol solution of furan (R_1 = R_2 = H) containing ammonium bromide as an electrolyte results in the formation of 2,5-dimethoxy-2,5-dihydrofuran[1,2,14-19], in 92% yield with respect to current, the hydrolysis of which gives a high yield of maleic dialdehyde, a valuable intermediate in the manufacture of synthetic fibres[20].

The electrochemical methoxylation of many α-alkylfurans[21,22], for example silvan (R_1 = H, R_2 = CH_3), and also of disubstituted derivatives such as 2,5-dimethylfuran (R_1 = R_2 = CH_3), which can be converted by methoxylation into a mixture of *cis*- and *trans*-isomers of 2-5-dimethoxy-2,5-dimethyldihydrofuran[22,23], has been studied. The corresponding dimethoxy-derivatives can be obtained by the electrochemical methoxylation of 5-ethyl-2-methylfuran and 2,5-diethylfuran[22].

Electrochemical methoxylation can occur not only as a result of the addition of a methoxy-group, but also as a result of substitution. A characteristic example of reactions of this type is the methoxylation of chloro- and bromo-furans[24]. Apart from reaction (1), substitution by a methoxy-group takes place. The electrochemical methoxylation of 2-bromo- and 2-iodo-furans (R_1 = Br or I; R_2 = H), 5-bromo-, 5-chloro-, and 5-iodo-furfurals (R_1 = Cl, Br, or I; R_2 = CHO), and the methyl ester of 5-bromopyromucic acid (R_1 = Br; R_2 = $COOCH_3$) has been achieved. In all cases the reaction yields trimethoxy-derivatives.

Electrochemical methoxylation takes places with a fairly high efficiency also in the electrolysis of certain other furan derivatives. For example, 2,5-dimethoxy-2,2-dihydrofurfuryl alcohol[21] and 2,5-dimethoxy-2,2-dihydrofurfuryl acetate[18,19,21] can be obtained from furfuryl alcohol (R_1 = H; R_2 = CH_2OH) and furfuryl acetate (R_1 = H; R_2 = CH_2OOCH_3) in yields of 77 and 81—86% respectively. Similarly methoxylation of furfural dimethylacetal [R_1 = H; R_2 = $CH(OCH_3)_2$] at the anode gives a high yield (with respect to the current), of 2,5-dimethoxy-2,5-furfural methylacetal[21]. Methyl pyromucate[25] and some of its derivatives[26-28], for example compounds with R_1 = CH_2NH_2 and R_2 = $COOCH_3$ or with R_1 = $(CH_3)_2CH$ and R_2 = $COOCH_3$, are methoxylated selectively with formation of the corresponding dimethoxy-derivatives. The presence of substituents in the 3- and 4-positions does not hinder the addition of methoxy-groups in the 2- and 5-positions, as can be seen from the following example:

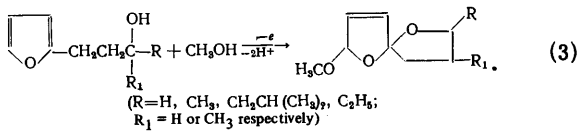


(2)

although the yield in this case does not in fact exceed 50%.[29]

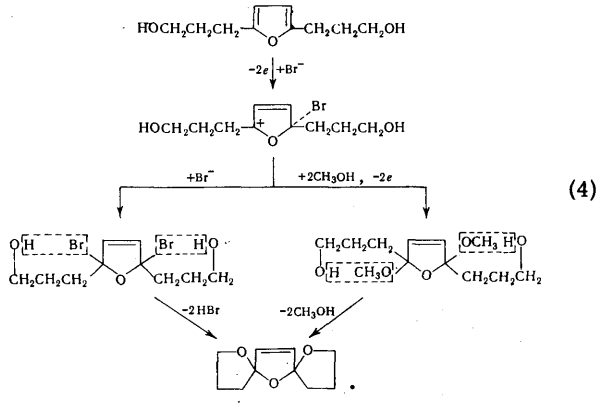
Ponomarev and Markushina[18,19,30-37] investigated the electrochemical alkoxylation of a large group of γ-furylalkanols and showed that, together with the usual addition

of the methoxy group, there is an intramolecular reaction accompanied by cyclisation:

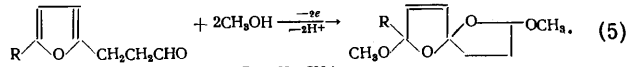

(R=H, CH_3, $CH_2CH(CH_3)_2$, C_2H_5; R_1 = H or CH_3 respectively) (3)

Thus the final products are the corresponding derivatives of 2-methoxy-1,6-dioxaspiro[4,4]non-3-ene. The electrochemical methoxylation of 1-(α-furyl)-3-propanol, 1-(α-furyl)-3-butanol, 1-(α-furyl)-5-methyl-3-hexanol, and a tertiary alcohol—1-(α-furyl)-3-methyl-3-pentanol—has been investigated. Polycyclic spirans are formed on electrochemical methoxylation of mono- and bi-cyclic alcohols[32,36,37]. An attempt at the electrochemical methoxylation of 2,5-di-(3′-hydroxyalkyl)furans led to interesting results[33]. For example, the methoxy-derivative could not be obtained at all from 2,5-di-(3′-hydroxypropyl)-furan. The anodic product of the electrolysis of the compound in methanol containing sodium bromide as the electrolyte is the *trans*-form of 1,6,8-trioxadispiro-[4,1,4,2]-tridec-12-ene.

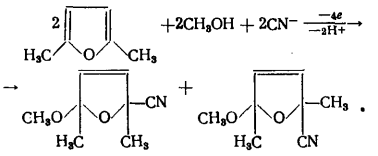
Intramolecular cyclisation is probably due to the involvement in the reaction of bromide ions and of the hydroxy-group of the initial alcohol. The intramolecular cyclisation reaction may proceed via the following mechanism:


(4)

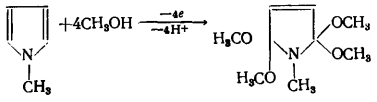
The electrochemical methoxylation of β-carbonyl derivatives of furans is extremely interesting. For example, the electrochemical methoxylation of aldehydes containing the furan ring makes it possible to obtain high yields of derivatives of 2,7-dimethoxy-1,6-dioxaspiro[4,4]non-3-ene[38]:


(R = H, CH_3) (5)

The yields of heterospirans vary from 53 to 76%. These products are of interest as biologically active preparations, in particular some of them exhibit a tranquilising activity[38]. If the methanol solution of the heterocyclic compound contains a readily oxidised anion, the electrolysis may be accompanied by the formation at the annode of a product containing two different substituents. For example, the electrolysis of a methanol solution of 2,5-dimethylfuran containing sodium cyanide gives a 74% yield of *cis*- and *trans*-2-cyano-5-methoxy-2,5-dimethyl-2,5-dihydrofurans[39]:


(6)

Whereas in the electrochemical methoxylation of furan derivatives two methoxy-groups add on as a rule, in the electrolysis of methanol solutions of *N*-methylpyrrole a tetra-substituted derivative is formed at the anode—2,2,5,5-tetramethoxy-1-methyl-3-pyrroline[40]:


(7)

2,6-Dimethoxypyridine undergoes electrochemical methoxylation whereby it is converted into 2,3,5,6-tetramethoxypyridine and 2,3,3,5,6-pentamethoxyazocyclohexa-1,4-diene[40,41].

Several studies have been made on the electrochemical alkoxylation of thiophen and its derivatives[42-44]. The alkoxylation of thiophen is accompanied by the formation of γ-dicarbonyl compounds[42], although in certain cases it is in fact possible to preserve the five-membered heterocycle. For example, 2,5-dimethoxy-2,5-dihydrothiophen can be obtained in 36% yield by the electrochemical methoxylation of thiophen[45]. The methoxylation of methyl 3-(5-methyl-2-thienyl)propionate also involves ring rupture and the formation of a sulphur-free product, which does however contain a methoxy-group: methyl 4,7-dioxo-uct-5-enoate[43]. The electrochemical methoxylation of 1-(3-thienyl)ethyl acetate also involves the removal of sulphur and the formation of 4-acetoxy-3-dimethyoxy-methylpent-2-ene-1-al dimethylacetal (46% yield)[44].

In conclusion, we must consider the alkoxylation of hydrogenated furan and thiophen derivatives—tetrahydrofuran and tetrahydrothiophen[46]. Methoxylation takes place in both cases with formation of α-methoxytetrahydrofuran and α-methoxytetrahydrothiophen in yields of 26 and 8.5% respectively on electrolysis of methanol solutions containing sodium methoxide.

The conditions governing the electrochemical ethoxylation of heterocyclic compounds probably do not differ significantly from those for methoxylation. This is indicated by experiments on the electrochemical oxidation of furan in ethanol[47].

III. ELECTROCHEMICAL ALKOXYLATION OF UNSATURATED AND AROMATIC HYDROCARBONS

Electrochemical alkoxylation of unsaturated hydrocarbons is more selective than the reactions involving heterocyclic compounds. The electrochemical methoxylation of aryl-substituted unsaturated hydrocarbons—styrene and its derivatives[48,49] and stilbene[49,50]—has been investigated in greatest detail. The electrochemical methoxylation of styrene gives a 20% yield of dimethoxyphenylethane[48]:

(8)

α-Methylstyrene and 1,1-diphenylethylene are converted respectively into the dimethyl ether of 1-methyl-1-phenylethylene glycol (15%) and the dimethyl ether of 1,1-diphenylethylene glycol[48] in 23% yield.

The electrochemical ethoxylation of styrene resulted in the formation of methane, ethane, the diethyl ether of styrene glycol, *meso*-1-4-diethoxy-2,3-diphenylbutane, and condensation products of acetaldehyde which the authors[49] believe to be formed as a result of decomposition of ethoxy-radicals. Studies on the electrochemical alkoxylation of stilbene[49,50] indicate the possibility of obtaining a satisfactory yield of dimethoxydiphenylethane.

Benzene does not undergo electrochemical alkoxylation, while its derivatives are methoxylated on electrolysis[51-56]. Benzyl methyl ether, 1-methoxy-1-phenylethane, and α-methoxyisopropylbenzene have been obtained in low yields by the electrochemical methoxylation of toluene, ethylbenzene, and cumene respectively[51]. The reactivity of alkylbenzenes in the alkoxylation reaction decreases in the sequence $C_6H_5CH(CH_3)_2 > C_6H_5C_2H_5 > C_6H_5CH_3$.

Interesting data have been obtained on the electrochemical methoxylation of 9,10-disubstituted anthracene derivatives[53]. On methoxylation of anthracene and 9,10-dimethylanthracene, the ratios of the *cis*- and *trans*-dimethoxy-derivatives are respectively 3:1 and 5:1. If diethyl-, dipropyl-, and diphenylanthracenes are methoxylated, the ratio of the *cis*- and *trans*-isomers changes in favour of the latter, approaching 1:1.

Reactions involving tetralin, indan, and diphenylmethane lead to the formation of the corresponding α-methyl ethers in low yields[55,57]. If the methanol solution of tetralin contains cyanides, then at anodic potentials of about 2.5 V electrochemical cyanation products[54], for example 6-cyanotetralin[56], appear in solution in addition to the methoxy-derivatives.

The electrochemical methoxylation of cycloalkenes yields the corresponding mono- and di-substituted derivatives[58]. For example, 1-methoxycyclohex-2-ene, 1,1-dimethoxycyclohexene[58], and in some cases 3-methoxycyclohex-1-ene[59] may be obtained from cyclohexene, while 1-ethylcyclohex-1-ene can give rise to 1-(1′-methoxyethyl)cyclohex-1-ene, 1-ethyl-3-methoxycyclohex-1-ene, and 2-ethyl-1-methoxycyclohex-2-ene[58]. The methoxylation of 2-methylpent-2-ene gives rise to three products: 3-methoxy-2-methylpent-1-ene, 2,3-dimethoxy-2-methylpent-1-ene, and 2,2-dimethoxypent-2-ene in an overall yield of 71%.[58] 3,4- and 3,6-dimethoxycyclohex-1-enes are formed as a result of the electrochemical methoxylation of cyclohexadiene[60]. A certain amount of the products of the addition of the methoxy-radical in the 1- and 4-positions are observed on electrolysis of the methanol solution of buta-1,3-diene[61,62], although in this case the methoxy-dimerisation reaction, which will be discussed below, is more typical.

As in some of the examples discussed previously, electrochemical methoxylation may result in the formation of bifunctional compounds owing to the addition of two different substituents to the hydrocarbon molecule. For example, electrolysis at the anode of methanol saturated with hydrogen chloride and ethylene results in the formation of chloromethoxyethane together with dichloroethane[63,64]:

$$C_2H_4 + CH_3OH + Cl^- \xrightarrow[-H^+]{-2e} CH_3OCH_2CH_2Cl. \qquad (9)$$

1-Hydroxy-4-methoxybut-2-ene can be synthesised by the electrolysis of a methanol solution of potassium hydroxide containing buta-1,3-diene[62,65].

IV. ELECTROCHEMICAL ALKOXYLATION OF COMPOUNDS WITH FUNCTIONAL GROUPS

A number of studies have been devoted to the electrochemical alkoxylation of organic acids. For example, electrochemical oxidation of *exo*- and *endo*-norbornane-3-carboxylic acid in methanol solution yielded methyl *exo*-norbornyl ether, while *exo*- and *endo*-5-norbornenecarboxylic acids give rise to 3-methoxynonatricyclene[66]. Methoxy-derivatives of hydrocarbons are formed in the electrolysis of methanol solutions of organic acids as a result of the replacement of the carboxy-group by a methoxy-group. For example, in the oxidation at the annode in methanol solution of acids with the general formula $o\text{-}XC_6H_4(CH_2)COOH$, where X = Cl, Br, or O_2, the methoxy-derivative $o\text{-}XC_6H_4(CH_2)_nOCH_3$ was detected together with the products of the anodic Kolbe condensation and certain other derivatives[67]. The yield of ether diminishes with increase of *n*. The substitution process can involve also the hydrogen atoms in the side chain. This is characteristic of phenylacetic acids[66]:

$$RC_6H_4CH_2COOH \xrightarrow[-CO_2,\ -H^+]{-2e,\ +CH_3OH} RC_6H_4CH_2OCH_3$$
$$\xrightarrow[-CO_2,\ -3H^+]{-3e,\ +2CH_3OH} RC_6H_4CH(OCH_3)_2$$
$$\xrightarrow[-CO_2,\ -H^+]{-4e,\ +3CH_3OH} RC_6H_4C(OCH_3)_3. \qquad (10)$$
(R=CH$_3$O, N(CH$_3$)$_2$)

The electrochemical alkoxylation of adamantane-1-carboxylic acid in a methanol solution of sodium methoxide results in the formation of 1-methoxyadamantane in 65% yield[68]. Under the same conditions, the methoxylation of adamantane-1-acetic acid leads to 3-methoxyhomoadamantane[69]. If the methanol solution of an unsaturated acid contains hydrogen chloride or bromide, then chlorine or bromine adds to the double bond together with the methoxy-group. Thus α-chloro- or α-bromo-β-methoxyphenylpropionic acid can be obtained from cinnamic acid[70]. Methoxylated products were detected also in the anodic Kolbe condensation of ω-hydroperfluorovaleric and ω-hydroperfluorooenanthic acids[71]. The principal products of the anodic oxidation of certain α-ketoacids RCOCOOH in methanol solutions are the methyl esters $RCOOCH_3$ (R = CH_3, C_2H_5, or n-C_3H_7), which are formed in yields of 65—81.5%.[72] The yield of esters increases in the following sequence in terms of R: $CH_3 > C_2H_5 >$ n-C_3H_7.

The possibility of the methoxylation [part of the Russian text is missing at this point (Ed. of Translation)].....the yield of methoxydioxan is 28%.[46]

Among nitrogen-containing organic compounds, most attention has been devoted to the alkoxylation of amines[17,40,73,74]. Electrochemical methoxylation of *NN*-dimethylaniline gave a mixture[46] of *N*-methoxymethyl-*N*-methylaniline and the product of more extensive alkoxylation—*NN*-(dimethoxymethyl)aniline—in proportions of 6:1:

$$C_6H_5N(CH_3)_2 \xrightarrow[-H^+]{-e,\ +CH_3OH} C_6H_5N(CH_3)(CH_2OCH_3) \xrightarrow[-H^+]{-e,\ +CH_3OH} C_6H_5N(CH_2OCH_3)_2. \qquad (11)$$

Similarly one can synthesise α-methoxy-*NN*-dimethylbenzylamine and *N*-methoxymethyl-*N*-methylbenzylamine from *NN*-dimethylbenzylamine and 3-methyl-2-phenyloxazolidine, 3-benzyloxazolidine, and *N*-methoxymethyl-*N*-methylbenzylamine from *N*-benzyl-*N*-methylethanolamine[40,74]. The electrochemical methoxylation of

cyclohexyl isocyanate takes place with a low yield of methoxylated products (20%) and seven different compounds, five of which proved to be methoxides, were identified in the mixture[74].

A few studies have been made on the electrochemical methoxylation of ethers. For example, in the electrochemical methoxylation of the dimethyl ether of resorcinol, 2,3,3,6,6-pentamethoxycyclohexa-1,4-diene is formed in 61% yield[76]. However, veratrol is methoxylated at the anode with a lower selectivity and yields four substances, including hexamethyl *cis,cis-o*-muconate—the product of the opening of the benzene ring[76]. In the electrochemical methoxylation of anisole[41,77] in an alkaline solution, *o*-, *m*-, and *p*-dimethoxybenzenes are formed in proportions of 39 : 3 : 58.[41] The reaction in an acid medium takes place in a more complex manner[77]. In this case, the electrolysis products are the methyl esters of *p*-methoxybenzoic (45.3%) and *o*-methoxybenzoic (4.5%) acids as well as the dimethyl esters of maleic (15.5%) and succinic (23.8%) acids.

The electrochemical alkoxylation of trimethylsilane has also been described[78]. The yield of alkoxytriethylsilane in the electrolysis of an ethanol solution of triethylsilane varies in the range 30—80%. Attempts at electrochemical alkoxylation in *t*-butyl alcohol were unsuccessful.

V. ELECTROCHEMICAL ALKOXYDIMERISATION

In some cases electrochemical alkoxylation is accompanied by dimerisation with formation of dimethoxy-derivatives of compounds with twice as many carbon atoms as the starting material. For example, a dimeric product—*meso*-1,4-diethoxy-2,3-diphenylbutane—is formed in the electrolysis of an ethanol solution of styrene at the anode together with the ethoxylation product (the diethyl ether)[49,79]:

$$2C_6H_5CH{=}CH_2+2C_2H_5OH \xrightarrow[-2H^+]{-2e} C_6H_5CH(OC_2H_5)-CH_2CH_2-CH(OC_2H_5)C_6H_5. \qquad (12)$$

The electrolysis of a methanol solution of *cis*-cyclopropane-1,2-dicarboxylic acid results in the formation of a mixture of dimeric products—dimethyl ester of bicyclopropyl-2,2-dicarboxylic acid and the methyl ester of cyclopropane-1,2-dicarboxylic acid[80]. A number of studies in recent years were specially undertaken to investigate the conditions governing the alkoxydimerisation reaction and the methods for the electrochemical synthesis of alkoxydimers[61,62,65,79,81,82].

Electrochemical methoxylation of buta-1,3-diene can give rise under certain conditions to three isomeric dimethoxyoctadienes[79,83]: *trans, trans*-1,8-dimethoxyocta-2,6-diene, *trans*-1,6-dimethoxyocta-2,7-diene, and 3,6-dimethoxyocta-1,7-diene. In other investigations[61,62,65], 1,6-dimethoxy-2-vinylhex-4-ene was detected in addition to the first isomer. However, the product yields do not exceed 15%. Apart from the products mentioned, two isomeric dimethoxydodecatrienes were detected in an overall yield of 11%.[83] Methoxydimers are obtained in somewhat higher yields in the electrolysis of arylated olefins—styrene, α-methylstyrene[83], and isoprene[84]—as well as vinyl ethers[81,85]. In the last case, the reaction has been investigated for a fairly large number of systems:

$$2R_1O-\underset{R_3}{\overset{}{C}}=\underset{R_4}{\overset{}{C}}-R_2+2R_5OH \xrightarrow[-2H^+]{-2e} R_1O-\underset{R_3}{\overset{OR_5}{C}}-\underset{R_4}{\overset{R_2}{C}}-\underset{R_4}{\overset{R_2}{C}}-\underset{R_3}{\overset{OR_5}{C}}-OR_1, \qquad (13)$$

where $R_1,\ldots,R_5$ are C_nH_{2n+1} groups with $n = 1-8$ for R_1, $n = 0-8$ for R_2-R_4, and $n = 1-4$ for R_5; R_1 can also be a five- or six-membered cycloalkyl group.

Together with dimerisation, there is simple addition of alkoxy-groups to the double bond. The yield of products then exceeds the yield of methoxydimers, although in some cases, for example, for ethyl vinyl ether, it reaches 51%.[83]

A methoxydimer—1,1-dimethoxy-2,2′-bisindanyl—can be obtained in 38% yield by the anodic oxidation of indene in methanol[83].

Finally, we must consider the anodic coupling reaction with formation of dimethoxy-derivatives occurring when alcoholic solutions of two different unsaturated hydrocarbons are electrolysed[82]. For example, the electrolysis of a methanol solution of styrene and ethyl vinyl ether results in the formation of a methoxydimer—4-ethoxy-1,4-dimethoxy-1-phenylbutane:

$$C_6H_5CH{=}CH_2+H_2C{=}CHOC_2H_5+2CH_3OH \xrightarrow[+2H^+]{-2e} C_6H_5CH(OCH_3)-CH_2CH_2-CH(OCH_3)OC_2H_5, \qquad (14)$$

1-Ethoxy-1,4-dimethoxy-4-phenylpentane has been synthesised in this way from α-methylstyrene and ethyl vinyl ether.

VI. CONDITIONS GOVERNING THE ALKOXYLATION AND ALKOXYDIMERISATION REACTIONS

The mode of the alkoxylation reaction and the nature and yields of products depend largely on the nature of the anode material, the electrolyte, the concentrations of the initial organic compounds, the current density, the anode potential, and the solution temperature. Systematic studies designed to compare the roles of these factors have not been made. However, certain largely qualitative generalisations can be made from the available data.

Electrochemical alkoxylation and alkoxydimerisation have been carried out at anodes made of platinum[17,22,23,40,48-50,52,54,55,57,58,60-62,65,68,73,74,76,85] and charcoal or graphite[5,18,19,24,30-38,43-46,75,79,82,83]. Platinum[66,74], graphit[82], nickel[18,19,40,43,61,62,65,47] or mercury[22,60] have been used as the cathode materials. Probably in the electrochemical alkoxylation of heterocyclic compounds, fairly high yields of products may be achieved at both platinum and graphite anodes. On the other hand, in the vast majority of the experiments on the electrochemical alkoxylation of hydrocarbons and organic compounds with functional groups platinum anodes were used.

The choice of electrolyte constitutes a very important problem. Electrochemical alkoxylation of heterocyclic compounds takes places most efficiently in alcoholic solutions of bromides, mainly ammonium bromide. Attempts to employ as electrolytes alcoholic solutions of nitrates, carboxylic acid salts, and sulphuric acid inevitably resulted in a lower yield of alkoxy-derivatives. The specific role of bromide in the electrochemical alkoxylation of heterocyclic compounds has been discussed by a number of workers[2,24,33,41]. Alcoholic solutions of alkalis and alkoxides can be recommended for the electrochemical alkoxylation of hydrocarbons[49,61,62,65] and tertiary amines[17]. Attempts to employ bromides as electrolytes in the electrochemical alkoxylation of unsaturated hydrocarbons lead to the formation of bromo-derivatives.

An important process parameter is the anodic current density. Electrochemical alkoxylation is carried out over

a fairly wide range of anodic current densities—from 1 to 10 A dm^{-2}. The ratio of the alkoxylation and alkoxydimerisation products depends to a considerable degree on the anodic current density when these reactions can occur simultaneously. Experimental data show that the yield of alkoxydimerisation products as a rule increases with decrease of anodic current density. Anodic current density can also influence the proportions of the isomers of the alkoxydimers. For example, in the electrochemical methoxylation of buta-1,3-diene an increase of anodic current density entails an increase in the yield of the linear dimer 1,8-dimethoxyocta-2,6-diene in a mixture with the branched isomer 1,6-dimethoxy-2-vinylhex-4-ene[62].

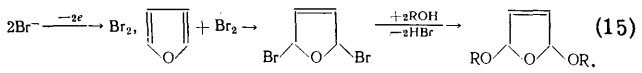
The mode of reaction is influenced significantly by the concentration of the initial organic compound. As a rule, when the alkoxylation reaction is accompanied by alkoxydimerisation an increase in the concentration of the initial organic compound tends to increase the rate of the latter[62].

Finally, we must consider the effect of the temperature of the solution electrolysed. In most cases, it is recommended that the electrolytic alkoxylation of heterocyclic compounds be carried out at low temperatures ranging from −20°C [1,14] to 25°C.[43] It is also useful to maintain low temperatures (between −10° and −15°C) when low-boiling reagents (for example buta-1,3-diene) are involved in the reaction in order to reduce their volatility and increase their solubility. It is not recommended that the alkoxylation and alkoxydimerisation reactions be carried out above 20—25°C, although the methoxylation of cyclohexyl isocyanate in the electrolysis of boiling methanol containing sodium methoxide has been described[75].

VII. THE MECHANISMS OF THE ALKOXYLATION AND ALKOXYDIMERISATION REACTIONS

The number of studies on the mechanisms of the alkoxylation and alkoxydimerisation reactions is much smaller than on their preparative applications. In the published studies, the mechanism of electrochemical alkoxylation is generally regarded as an aspect of the electrode processes (the nature of the primary stage, the adsorption of the reactants, etc.) or is treated from the standpoint of secondary chemical reactions (the mode of addition and substitution, structural effects, etc.). Studies dealing in detail and systematically with the problems of the secondary and primary reactions in electrochemical alkoxylation and alkoxydimerisation have not yet been made. The literature data on this question are often highly contradictory. This is largely caused by experimental difficulties, which are inevitable when electrochemical methods are employed to investigate the kinetics of electrode processes in non-aqueous media. Significant difficulties arise also owing to changes in the surface of the anode over a period of time—a specific deactivation effect is characteristic of many anodic alkoxylation processes[44,62,80]. Electrochemical measurements are limited as a rule to the recording of polarisation curves[17,74,86,87]. On the other hand, the interpretation of the mechanism solely on the basis of an analysis of stable electrolysis products, which is done in the majority of investigations[41,88], makes the reaction mechanisms thus devised somewhat arbitrary[88,89]. As a result the mechanisms of the alkoxylation and alkoxydimerisation reactions remain on the whole to a considerable degree controversial. We shall consider certain modern ideas in this field.

The generally accepted view is that the alkoxylation reaction proper is the secondary chemical reaction which follows the discharge of the electrochemically active species at the electrode. However, different investigators hold divergent views concerning the nature of this species. As already mentioned, in the first studies on the methoxylation of furan, it was established that the reaction takes place most efficiently when bromide salts are employed as the electrolytes. On this basis, it was concluded in a number of investigations[2,5,15,19,24,33], that the initial reaction stage is the discharge of the bromide ion. This view is held, for example, by Ponomarev and Markushina[9,33], who suggest that the alkoxylation of furan derivatives proceeds via three stages. The first involves the oxidation of the bromide ion with formation of molecular bromine, in the second bromine undergoes 1,4-addition to the ring, and in the third dibromohydrofuran is alkoxylated chemically with elimination of HBr:



(15)

Kochetkov et al.[90] assume an analogy with chemical alkoxylation in the presence of bromine, where the initial stage is two-step electrophilic addition of Br_2. Sokolov and Giller believe that the primary step in the electrochemical methoxylation of furans in the presence of ammonium bromide is the formation of atomic bromine and its subsequent recombination to molecular bromine, which is in fact responsible for the methoxylation proper in the bulk of the solution[24]. A similar point of view has been largely adopted in studies by certain Japanese investigators[52], who assume that the discharge of the anion, regardless of its nature, is the initial reaction step. In contrast to the previous mechanism, Japanese investigators believe that the process may be described by the following consecutive reactions:

$$X^- \rightarrow X^\cdot + e\,(A);\ RH + X^\cdot \rightarrow HX + R^\cdot \qquad (B) \qquad (16)$$
$$CH_3OH \rightarrow CH_3O^\cdot + H^+ + e\,(C);\ R^\cdot + CH_3O^\cdot \rightarrow CH_3OR\ (D).$$

It is suggested that reaction (16B) is rate-determining. A characteristic feature of this mechanism is the electrochemical step involving the anodic oxidation of an alcohol molecule with formation of a $CH_3O\cdot$ radical. Methoxylation takes place homolytically as the recombination of $CH_3O\cdot$ and a radical formed from the substrate molecule via reaction (16B). Possibly in some cases, for example in halogen-containing electrolytes, this mechanism is acceptable but it can hardly be general. In fact the yield of methoxy-derivatives of furan is higher in solutions of bromide salts, but these derivatives are formed also in electrolytes containing NH_4NO_3, $NaNO_3$, sodium formate[17,91], sulphuric acid[61,62,91], alkalis[52,65,84], boron trifluoride-ether[91], cyanides, perchlorates[39,52,74], and other compounds[52]. The discharge of the anions of such electrolytes, for example ClO_4^-, F^-, etc., requires much higher positive potentials than those which actually obtain in the alkoxylation or alkoxydimerisation reactions. Naturally the step (16C) is ruled out when the electrolyte is a methoxide. Thus the mechanisms postulating as the initial step the direct electrochemical oxidation of the alcohol at very low positive potentials are more acceptable and undoubtedly more general.

Regardless of the conflict between the views concerning the nature of the electrochemical stage, the involvement of the methoxy-radical in the reaction is postulated by the

vast majority of investigators. However, the assertion that the electrochemical oxidation of alcohols generates the corresponding alkoxy-radicals is frequently made without sufficient evidence, solely on the basis of the observed formation of ethers. An attempt at a quantitative approach to this problem was made by Tsutsumi and coworkers[51], who showed that the relative reactivities of many aromatic compounds in electrochemical alkoxylation is fully consistent with Szwarc's observations[92] on their behaviour in free-radical reactions. A further development of this approach, within the framework of mechanism (16), is illustrated by the work of Sasaky et al.[52], who investigated the reactivity of alkylbenzenes in the electrochemical synthesis of α-substituted methyl ethers under various conditions. They established a linear relation between the current yield and the heat of reaction (16B) (rate-limiting step) calculated from thermochemical data. They believe that this finding is consistent with Semenov's law of the proportionality between the activation energy and enthalpy[93] for radical reactions and therefore confirms the validity of the homolytic mechanism. Since such views have gained wide acceptance recently[55,94], note should be taken of the methodological error which they involve.

In the first place the current yield of methoxy-derivatives in various electrolytes cannot be regarded as equivalent to the relative reactivity (the rate constant for the reaction between X· and RH), since the rate of formation of X· and their "actual" concentration determined by the partial oxidation current [stage (16A)] are not taken into account. Since the potential was not measured in the electrolysis and the reaction was carried out galvanostatically, the feasibility of reaction (16A) in all the cases investigated (X^- = F^-, ClO_4^-, OH^-, Cl^-, etc.) becomes doubtful. The application of concepts of homogeneous kinetics to this reaction, which the authors themselves regard as heterogeneous[52], also appears incorrect.

It is not the first time that attempts have been made in the literature to employ thermochemical data in order to establish the mechanisms of electrode reactions. The error of this approach has been demonstrated by Conway and Vijh[95]. Moreover, the validity of the "Semenov—Polanyi rule" cannot alone be regarded as a criterion of the validity of the homolytic mechanism, since it is a special case of the Brønsted equation or "the principle of the linearity of free energies", which is valid for many classes of chemical reactions regardless of their mechanism[96]. The above critical comments do not, however, refer to the actual conclusion that the stage involving the formation of the ether is homolytic. This conclusion is adhered to by the majority of investigators of this reaction. According to Inoue and Tsutsumi[48], only homolytic substitution can result in the formation also of certain side products of the oxidation of alkylbenzenes in alcoholic media, for example dimeric compounds.

The possibility of forming alkoxy-radicals was confirmed in a study[97] of the oxidation of tertiary alcohols of the type $R_1R_2(C_6H_5)COH$ (R_1 and R_2 = CH_3, C_2H_5, and iso-C_3H_7). The authors of this investigation, who carried out the electrolysis in aqueous dioxan solutions of the alcohols, observed a high yield of ketones (80—90%) and detected dimeric gaseous products. These products were interpreted as resulting from the formation of t-alkoxy-radicals by the reaction

$$R_1R_2PhCOH \xrightarrow[-H^+]{-e} R_1R_2PhCO^{\cdot}. \qquad (17A)$$

Next, decomposition into ketone molecules and aliphatic radicals takes place:

$$R_1R_2PhCO^{\cdot} \begin{cases} \longrightarrow R_1COPh + R_2^{\cdot} \\ \longrightarrow R_2COPh + R_1^{\cdot}, \end{cases} \qquad (17B)$$

which then recombine or disproportionate according to the equations

$$R_1^{\cdot} + R_2^{\cdot} \begin{cases} \longrightarrow R_1R_1 + R_2R_1 + R_2R_2 \\ \longrightarrow R_1H + R_2H + \text{olefins}, \end{cases} \qquad (17C)$$

The intermediate formation of an alkoxy-radical in the reaction involving furan is also postulated in the electrolysis of solutions containing non-halide electrolytes[22,60].

Despite the fact that a homolytic mechanism is assumed in most investigations, there are also discrepancies as to the details of the process (if these are considered at all). Thus in many studies it is assumed that, under the conditions of electrolytic alkoxylation, the alcohol is oxidised in the molecular form[51,52,76,94]. However, comparative analysis of polarisation measurements and of the composition of the electrolysis products in the anodic methoxylation of tertiary amines in various electrolytes led to the conclusion[74] that the active species in the electrochemical stage proper is only the methoxide ion. The possibility of oxidising the alcohol at the anode in both molecular and anionic forms, depending on the acidity of the medium, is indicated by experiments on the alkoxylation of 1,3-dienes[84,98].

In early and also in certain recent investigations, the problem of whether the reaction is homogeneous or takes place on the surface of the electrode was ignored. Recently several special investigations on this question were made[17,40,52].

Sasaky et al.[99], who investigated the oxidation of methanol in the presence of $NaClO_4$, NaOH, and $NaOCH_3$ as supporting electrolytes, concluded that the methoxy-radical may diffuse far from the surface of the anode. This conclusion is based on the finding that the electrochemical oxidation is accompanied by the evolution of gas at the porous diaphragm separating the cathodic and anodic compartments. This fact is interpreted as follows:

$$CH_3OH_{ads} \rightarrow CH_3O^{\cdot}_{ads} + H^+ + e, \qquad (18A)$$

$$CH_3O^{\cdot}_{ads} \rightarrow CH_3O^{\cdot}_{bulk}, \qquad (18B)$$

$$2CH_3O^{\cdot} \xrightarrow{\text{disproportionation}} CH_3OH + HCHO. \qquad (18C)$$

However, these results were not confirmed by any other investigator. The mechanism proposed by Sasaky et al. can hardly be regarded as probably bearing in mind the instability of free $CH_3^{\cdot}$ radicals. The fact that the reaction

$$CH_3O \rightarrow HCHO + H \qquad (18D)$$

is endothermic [q = (−20)—(−40) kcal mole^{-1}] [93] is hardly an unambiguous indication that CH_3O· has sufficient stability for reactions (18B)—(18C), to occur as suggested by Sasaky et al.[99] Indeed, mechanism (18) itself shows that reaction (18D) does not constitute the only pathway for the removal of methoxy-radicals.

Many data indicating the formation of intermediate adsorbed radical products in the electrochemical oxidation of alcohols have been published[100-102]. The problems of the structure of these species have been the subject of special investigations in recent years by potentiostatic, galvanostatic, potentiodynamic, and radiochemical measurements[88,101-103]. However, these measurements were

made mainly in dilute aqueous solutions which precludes an unambiguous extrapolation of the results to alkoxylation conditions. This problem requires special consideration.

The oxidation of lower aliphatic alcohols in aqueous solutions up to high concentrations[100] has been intensively investigated in recent years in connection with the problem of fuel cells. As emphasised previously[88], the results of these investigations probably cannot be used for an unambiguous interpretation of the electrode processes in alkoxylation owing to the significant differences in reaction conditions. However, it would also be a mistake to ignore them completely (as is done in many investigations of the electrochemical alkoxylation), particularly since electrochemical synthesis of alkoxy-derivatives can take place also in aqueous alcoholic media[98].

A unanimous view on the mechanism of the anodic oxidation of alcohols in aqueous solutions does not exist either[101-103]. Electrochemical measurements at the electrode—alcohol solution boundary indicate the possible adsorption on the surface of the anode of a whole range of carbon-containing species characterised by different bonding energies with the surface. (For example: $\cdot C\begin{matrix}OH\\ \\ O\end{matrix}$, $\ddot{C}{=}O$, $\ddot{C}-OH$, and $\cdot CH_2OH$ in the oxidation of methanol and $CH_3\dot{C}HOH$ and $CH_3CH_2O\cdot$ for ethanol[104]). Some investigators[102] believe that in acid solutions methanol is oxidised via a stage involving the formation of the species $[COH]_{ads}$. Without special assumptions, such ideas are inconsistent with, for example, the results of the preparative electrolysis of acid alcoholic, including aqueous alcoholic solutions, which unambiguously demonstrate the homolytic addition of $CH_3O\cdot$ to the substrate molecule. According to the data of Podlovchenko et al.[105], the oxidation of methanol includes several parallel stages:

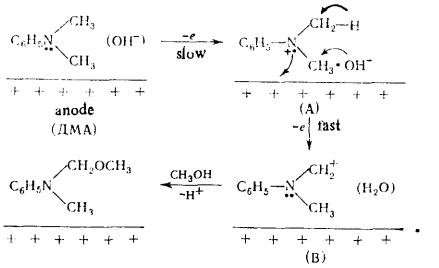
$$CH_3OH \rightarrow CH_3OH_{ads}\begin{cases}\longrightarrow SCS \rightarrow CO_2\\ \longrightarrow A_1 \rightarrow CO_2\\ \longrightarrow A_2 \rightarrow HCOOH\,(HCOO^-),\\ \longrightarrow A_3 \rightarrow H_2CO\end{cases} \qquad (19)$$

where SCS is a strongly chemisorbed substance and A_1, A_2, and A_3 are relatively weakly adsorbed species, whose composition has not been specified precisely. Analogous ideas were developed later by Breiter[106]. Although such mechanisms do not specify the nature of the adsorbed intermediates in the oxidation of the alcohol, they evidently allow a compromise with the results of electrochemical synthesis within the framework of the heterogeneous mechanism. Sasaky et al., who carried out the study on the electrochemical synthesis of alkoxybenzenes mentioned previously[52], also concluded that the reaction is heterogeneous. This conclusion is based on an analysis of kinetic data for the relation (which passes through a maximum) between the yield of the methoxy-derivative and the alcohol concentration.

In the study quoted previously[55], it was established that the products of the electrochemical synthesis of methoxy-derivatives of certain aromatic compounds differ significantly from the products of chemical methoxylation in the thermal decomposition of dimethyl peroxide (in particular, benzyl dimers, found among the products of the chemical synthesis, are not formed in the electrochemical synthesis). This anomaly can be readily explained if one postulates that the reaction layer is localised near the electrode (the high concentration of $CH_3O\cdot$ then prevents the dimerisation of benzyl radicals, promoting the formation of methoxy-derivatives).

The results of a study of the reaction involving amines lead to the conclusion that anodic alkoxylation is a heterogeneous process[17,40,73,74]. In particular, according to the data of Weinberg et al.[17,40], the adsorption of the substrate is an essential stage in the methoxylation of tertiary amines. Initially this conclusion was based on the structure of the electrochemical oxidation product of *NN*-dimethylaniline[40]. Subsequently it was confirmed by kinetic data[74]. The authors observed a fractional reaction order with respect to the amine, which is characteristic of the adsorption of substrate molecules in accordance with the Temkin or Freundlich isotherm[107]. Convincing evidence in support of the adsorption of the 1,3-diene under the conditions of anodic alkoxylation was also obtained by Zhurinov et al.[98]

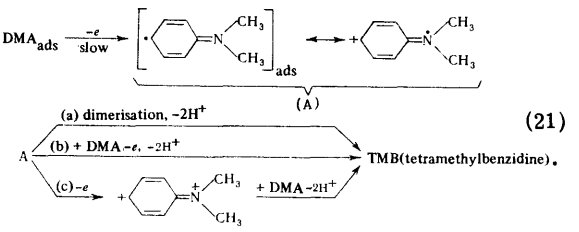
A number of studies carried out in recent years[88,103] also involved the investigation of the electrochemical behaviour of the substrate at the anode. The half-wave potentials for the oxidation of substances used in the alkoxylation reactions demonstrate the possibility, in principle, of oxidising many of them in the range potentials in which electrochemical synthesis is usually carried out. The results of studies by Eberson and coworkers[108-111] and also other workers[112-114] show that many electrochemically generated radicals may be oxidised further at their formation potentials. These data have led some investigators to hypotheses concerning the involvement of the substrate, including its ionised form, in the reaction[17,40,73,74]. For example, according to Weinberg and Reddy[17], the alkoxylation of tertiary amines proceeds via a stage involving the oxidation of the adsorbed amine molecules. Analysis of the Tafel sections of the polarisation curves and also of the potential—time relations under galvanostatic conditions led the authors to the conclusion that the molecule is oxidised electrochemically in steps. In the first, rate-limiting stage, one electron is abstracted with formation of a radical-cation. This is followed by a rapid stage with further one-electron oxidation of the radical-cation A and solvolysis with formation of the methoxy-derivative:



(20)

The wide variety of reaction products can be accounted for within the framework of this mechanism taking into account the pH of the electrolyte. The basicity of the solution promotes the deprotonation of the adsorbed radical-cation A.

In the absence of deprotonation facilitated by the hydroxide ion, the radical-cation A can enter only into the dimerisation reaction according to the equations



(21)

Kinetic data do not allow a choice between the three versions (a), (b) and (c). Other workers who investigated this reaction[74] also postulate the involvement of ionised intermediates in it, but they assume that the adsorbed radical and not the aniline molecule is oxidised. Smith and Mann[74] believe that the initial stage is the electrochemical oxidation of the methoxide anion to $CH_3O\cdot$, which dehydrogenates the amine moiety in the side chain:

$$CH_3O^- - CH_3O\cdot + e;\ 2CH_3O\cdot + 2PhCH_2N(CH_3)_2 \xrightarrow{-2CH_3OH} \underset{(I)}{PhCH_2-\overset{\cdot}{\underset{|}{N}}(CH_2)-CH_3} + \underset{(II)}{PhCHN(CH_3)_2}.$$

Methoxylated products are obtained as a result of the solvation of the radical-cations (III) and (IV) formed in the oxidation of the radicals (I) and (II) at the electrode:

$$\text{(I) or (II)} \xrightarrow[\text{anode}]{-e} \underset{(III)}{PhCH_2\overset{+}{\underset{|}{N}}(CH_2)-CH_3} \text{ or } \underset{(IV)}{PhCH\overset{+}{N}(CH_3)_2},$$

$$\text{(III) or (IV)} + CH_3O^- \rightarrow \underset{(V)}{PhCH_2\underset{|}{N}(CH_2OCH_3)-CH_3} \text{ or } \underset{(VI)}{PhCH\underset{|}{N}(OCH_3)(CH_3)_2}. \qquad (22)$$

The preferential formation of compound (V), which was also noted by Weinberg and Reddy[17], is attributed to the higher stability of compound (II) compared with (I). The hypothesis of the electrochemical oxidation of the substrate as a necessary stage in alkoxylation has also been adopted by certain investigators for furan derivatives[22,60]. This pathway is adopted, as an alternative to the purely homolytic mechanism, for the reaction with aromatic compounds[55]. The mechanism is analogous to that discussed above and involves the oxidation at the electrode of the radical generated in the homolytic deprotonation of the substrate molecule by the electrochemically generated methoxy-radical:

$$RH \xrightarrow{CH_3O\cdot} R\cdot \xrightarrow[\text{anode}]{-e} R^+ \xrightarrow{CH_3O^-} ROCH_3. \qquad (23)$$

Similar views have gained acceptance for the mechanism of the formation of ethers. This process is frequently accompanied by the Kolbe reaction[67,115-119] and proceeds as follows[18]:

$$RCOO^- \xrightarrow{-e} RCOO\cdot \xrightarrow{-CO_2} R\cdot \xrightarrow{-e} R^+ \xrightarrow[-H^+]{CH_3OH} ROCH_3. \qquad (24)$$

Wladislaw and Viertler, who investigated the successive anodic oxidation of certain phenylacetic acids, arrived at the same conclusion. They believe that the acid molecule undergoes two-electron oxidation at the anode[119].

However, it should be noted that in many studies the formation of carbonium ions is postulated only on the basis of the formal possibility of the oxidation of substrate molecules. For a correct solution of this problem, it is necessary to carry out electrolysis in each case at a measured potential in combination with the study of the electrochemical behaviour of the substrate itself. This problem has been discussed in greater detail in two reviews[88,103].

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Mendeleev Institute of
Chemical Engineering,
Moscow

U.D.C. 547.91:547.92

Chemical Defects in Macromolecules of Heterounit Polymers

V.V.Korshak

This review discusses reasons for the appearance of chemical faults in macromolecules during the preparation of polymers by addition polymerisation or polycondensation and as a result of substitution, oxidation, and other reactions of polymers. The presence of anomalous monomer units in chemically imperfect macromolecules leads to the formation of heterounit polymers, and their presence in the latter exerts a great influence on the chemical and physical properties of the polymers. A list of 198 references is included.

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I. CHEMICAL DEFECTIVENESS OF MACROMOLECULES

The dependence of the properties of polymers on their structure is one of the most important problems of polymer science, to whose solution a large number of investigators—both chemists and physicists—have directed their efforts. The Reviewer has adduced many examples of quite clear relations between structure and such properties of polymers as heat resistance and thermal stability[1]. It was found that, although the structure of a given polymer and its inherent combination of chemical and physical properties are determined by the fundamental structure of the monomer unit, a significant influence is exerted by the presence of anomalous units, which are responsible for the "chemical defectiveness of the macromolecular structure"[2-5]. This exhibits some analogy with the physics of solids, where the currently favoured theory is that the imperfection of the physical structure is the most important factor determining the real strength of any solid, including of course polymers[6,7].

The present Review aims to assess the significance of the chemical imperfection of macromolecules as a factor in determining the dependence of the properties of polymers on their structure. The Reviewer would also like to direct the attention of research workers to the finer details of the structure of macromolecules, and to show their value in establishing the dependence of the properties of polymers on structure.

The method generally adopted at present for representing polymer macromolecules indicate the structure only of the main component, whose repetition leads to formation of the macromolecular chain, as shown for instance by the formula of poly(vinyl chloride) $-[CH_2-CHCl]-$. All other structural features, usually designated the microstructure of the polymer—the nature of the end groups, the presence of branches and their number and size, the presence of abnormal monomer units differing in some way from the main units forming the polymer chain, the sequence of alternation of abnormal and normal polymer units, the spatial arrangement of the units and groups (the stereochemistry of the monomer unit and of the macromolecule), etc.—are incapable of representation by this method. This is probably one reason for the disregard of many important structural details of macromolecules, which are extremely significant for an understanding of the relation between the structure of polymers and their properties.

The importance of establishing the structure of the monomer unit and the relative arrangement of units in the macromolecule for an understanding of the properties of polymers was first appreciated by Harries[8] and Lebedev[9], and was systematically explored for a large number of polymers by Staudinger[10], Marvel[11], and other workers. Staudinger showed that the monomer units in the polystyrene macromolecule are linked in a uniform sequence[12]. Marvel[11] showed, with many different polymers as examples, that the same regular arrangement of monomer units is the fundamental law of the construction of macromolecules by polymerisation.

Further development of methods of investigation and a deepening knowledge of polymers led to our realisation that, together with the regular sequence of monomer units, there are several stereochemical and structural factors that are important for an understanding of the structure and the properties of polymers. Present-day methods of synthesising polymers are always accompanied by various types of side-reactions, leading to the formation in the polymer chain of a larger or smaller number of abnormal monomer units of various kinds, differing in some way from the main units. Cases have recently become more and more frequent in which certain apparently minor structural details of a polymer molecule actually have a very significant effect on the whole set of physical and chemical properties characterising the given polymer. Close study reveals that this is due to chemical defects in the macromolecules resulting from the presence of abnormal monomer units[2-5].

Abnormal monomer units influence the properties of the polymer as structural components of the macromolecule, their presence leading to a change in the polar effects between atoms both in this unit and in adjacent and sometimes even fairly remote neighbours, which influences the chemical properties of the polymer; they also make their contribution to the flexibility of and intermolecular interaction between the macromolecules, either weakening or strengthening it, but also influencing the character and degree of order of the macromolecules, which affects the physical properties of the polymer. Ideas based solely on the study of homopolymers are therefore no longer adequate for a proper understanding of the relations between the properties and the structure of polymers. A new approach is required, which would take into account all the aspects of the structure of polymeric molecules. In this connection with concept of "heterounit" polymers is of

fundamental significance, being the main type of polymeric structures which arises from the introduction of abnormal units into the macromolecule.

The chemical defectiveness of the macromolecular structure characteristic of heterounit polymers can be produced intentionally, as in all kinds of copolymerisation and polycondensation, as well as by substitution in a polymeric molecules, which are widely used for modifying the properties of polymers. In these cases, where we control the processes and can choose a desired extent of change in the polymer, the equivalent degree of chemical imperfection can vary within very wide limits.

Cases in which chemical imperfection arises spontaneously, contrary to our wishes, during the synthesis or the modification of a polymer, are far more important. Chemical defectiveness of a macromolecular structure usually results from the inclusion in the polymer chain of abnormal monomer units, having some kind of structural difference from the chief units. In several cases very reliable evidence has been obtained of the presence of abnormal units in polymer macromolecules. Still more cases are known in which there are weighty grounds for assuming their presence.

In every chemical reaction the main product is accompanied by a larger or smaller quantity of secondary products. The yield of the main product usually shows the proportion of the main reaction. The secondary products are removed on purification, and thus do not affect the quality of the main product, merely diminishing its yield. In the formation of polymers, however, all secondary products remain as an integral part of the polymer in the form of abnormal units, and this is one reason for its chemical defectiveness. Therefore, although we write the general formula for a polymer as $[M]_x$, where M represents a monomer residue, this is an idealised formula. It would actually be more correct to represent the structure of a real polymer by a formula such as $[-[M]_m-[A]_n-]_x$, where A is an abnormal unit and M a normal unit [3,5].

The types of chemical defectiveness of macromolecules and the ways in which the corresponding abnormal monomer units arise can be indicated briefly.

1. Abnormal units resulting from cross-links, side-chains, branches, and other abnormal structures.
2. Differences during addition polymerisation or polycondensation in the coupling of units "head to head" or "head to tail".
3. Isomerisation of monomer units during addition polymerisation and polycondensation.
4. Appearance of abnormal units owing to differences in the configuration of asymmetric carbon atoms forming the macromolecular chain ("tacticity").
5. Formation of abnormal units resulting from differences in the configuration of groupings having central, axial, and planar asymmetry.
6. Differences in geometrical isomerism of units formed by the polymerisation of dienes, and also those containing disubstituted rings.
7. Differences in the structure of monomer units resulting from conformational asymmetry and hindered rotation of the units.
8. Abnormal units resulting from incomplete trimerisation in the polycyclotrimerisation of diynes.
9. Abnormal units as the residue of incomplete formation of a carbocyclic or a heterocyclic ring during polycyclisation or polycyclocondensation.
10. Appearance of abnormal units as a result of copolymerisation and copolycondensation.
11. Abnormal monomer units resulting from chemical reactions of units in the macromolecule (chlorination, oxidation, dehydration, etc.).

The abundance of published data more or less closely connected with the present problem does not permit a complete review of the whole literature on this question, and only individual researches can be mentioned below as examples illustrating the principles under discussion.

II. MODES OF APPEARANCE OF ANOMALOUS MONOMER UNITS IN MACROMOLECULES OF HETEROUNIT POLYMERS

All the known syntheses and transformations of polymers are accompanied by various side-processes leading to the appearance of abnormal monomer units and the formation of heterounit polymers. Among reactions leading to the appearance of abnormal units are the recombination of macroradicals, intra- and inter-molecular chain transfer, formation of an atactic chain structure, isomerisation of monomer units, various types of copolymerisation and copolycondensation, various substitutions in the chain, and also various secondary processes occurring during polymerisation and polycondensation [3,5]. We use individual examples to examine the ways in which chemical imperfection appears in macromolecules during the synthesis and the transformation of polymers.

1. Appearance of Abnormal Monomer Units during Polymerisation

The polymerisation of unsaturated compounds by a radical or other mechanism is accompanied by such reactions as the recombination of macroradicals and also intramolecular and intermolecular chain transfer, isomerisation of the monomer unit, etc., leading to the formation of abnormal units. In the first case the recombination

$$(-CH_2CHX)_m-CH_2CHX^{\cdot} + {}^{\cdot}CHXCH_2-(-CHXCH_2-)_n- \rightarrow (-CH_2CHX-)_m-CH_2CHX-CHXCH_2-(-CHXCH_2-)_n$$

results in the appearance of the anomalous group $-CHX-CHX-$ in the chain. In the second case branches and side-chains of various lengths appear as a result of chain transfer.

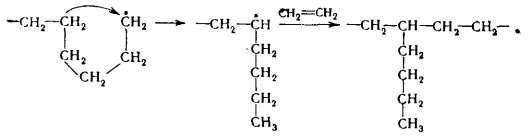
The simplest example of such a polymer containing abnormal monomer units formed during polymerisation is high-pressure (low-density) polyethylene, in which the presence of a considerable number of small, and a small quantity of large, side-chains has been reliably demonstrated. As a result, of course, the macromolecule of such a polymer contains a considerable quantity of units having the structure

$$\cdots-CH_2-\underset{\vdots}{CH}-\cdots \quad \text{or} \quad \cdots-CH_2-\underset{R}{CH}-\cdots .$$

Such units arise from chain transfer, and their presence must therefore be assumed in all polymers obtained by radical polymerisation. The presence of such units in some polymers of this type has been proved experimentally [13]. The formation of long side-chains is a result of intermolecular chain transfer:

$$-CH_2-CH_2-CH_2-CH_2- \xrightarrow{R^{\cdot}} -CH_2-CH_2-\dot{C}H-CH_2- \longrightarrow$$
$$\xrightarrow{CH_2=CH_2} -CH_2CH_2-\underset{\displaystyle CH_2-CH_2-}{\overset{\displaystyle |}{CH}}-CH_2- .$$

Short branches are formed by intramolecular chain transfer [14]:



Butyl side-chains are formed in this way. Ethyl groups, however, are produced by the reaction

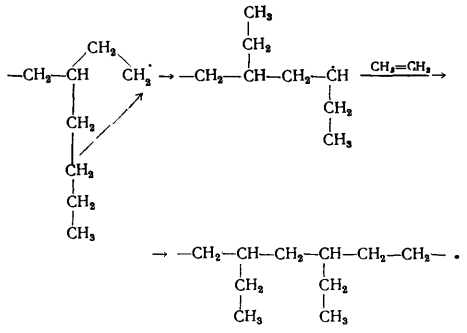
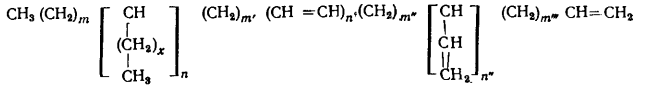


Table 1. Presence of abnormal groups in polyethylene [15].

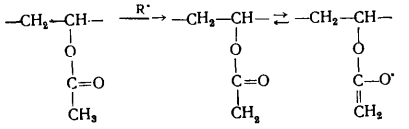
Abnormal group	Abnormal groups per 1000 carbon atoms in	
	low-density (high-pressure) polyethylene	high-density (low-pressure) polyethylene
Methyl (total content) including end-groups	21.5	3.0
Methyl (in side-chains)	4.6	~2.0
Ethyl (in side-chains)	2.5	—
Ethylenic bonds including (% of bonds)	14.4	1.0
$R-CH=CH_2$ type	0.6	0.7
$RR'C=CH_2$ type	15.0	43.0
$R-CH=CH-R'$ type	68.0	32.0
	17.0	25.0

As a result of this, polyethylene obtained by radical polymerisation (low-density polyethylene) contains such groups as ethyl and butyl, together with long side-chains [13]. Furthermore, its macromolecule contains double bonds both in the main chain and in side-chains. Table 1 gives the results of an investigation of the structure of polyethylene [15]. Consequently the actual structure can be represented by the formula



where in low-density polyethylene $n = 20-40$, $n' = 1$ or 2, $n'' = 1$ or 2, and $x = 0-1000$; and in high-density polyethylene $n = 1$ or 2, $n' = 1$ or 2, $n'' = 1$ or 2, and $x = 0-10$. Determination of the presence of side-chains in several samples of high-pressure polyethylene showed that the relative degree of branching decreased as the chain grew, although the content of methyl groups per macromolecule increased (Table 2) [16].

Investigation of the copolymerisation of ethylene with vinyl acetate [14] showed that the degree of branching of the copolymer increased with rise in temperature (Fig. 1). In the case of poly(vinyl acetate) branchings of the polyethylene type may be accompanied by branchings as a consequence of chain transfer via the acetyl group [17]:



which leads to the formation of readily hydrolysable units having the structure

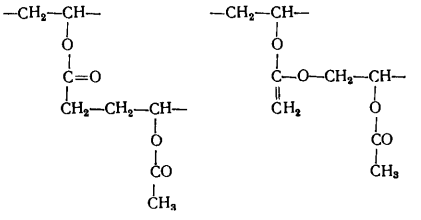


Table 2. Content of methyl groups in various specimens of high-pressure polyethylene.

Mol. wt.	No. of CH_3 per		Mol. wt.	No. of CH_3 per	
	1000 C	macromolecule		1000 C	macromolecule
1700	48	5.5	24000	31	52.0
2400	44	7.1	28000	28	54.0
4000	42	11.4	32000	23	52.0
5300	40	14.5	48000	20	67.2
6600	38	17.5	53000	18	67.5
19000	37	48.5	76000	18	93.5
21000	33	48.5			

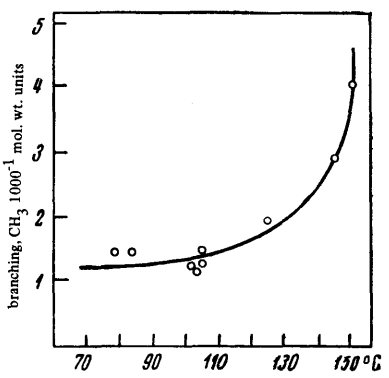
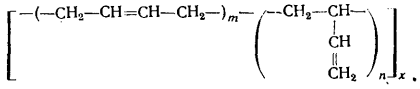


Figure 1. Effect of temperature of polymerisation on branching of a copolymer of ethylene with vinyl acetate.

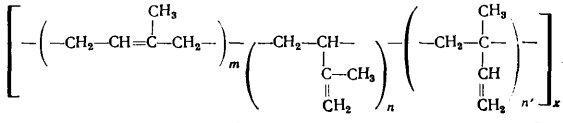
A similar branching reaction is possible also with other esters of poly(vinyl alcohol), as also with polyacrylic and polymethacrylic esters.

The polymerisation of dienes is extremely sensitive to conditions, so that polymers of varied structure can be obtained. Dolgoplosk and Tinyakova[18] examined the mechanism of the polymerisation of dienes and the microstructure of the resulting polymer chain, and showed that the polymerisation of butadiene may lead to the formation of polymers containing monomer units linked together at the 1,2- and 1,4-positions, of *cis*- and *trans*-configuration, and also cyclic units and other structures. With polymers of isoprene 3,4-units may also appear[19].

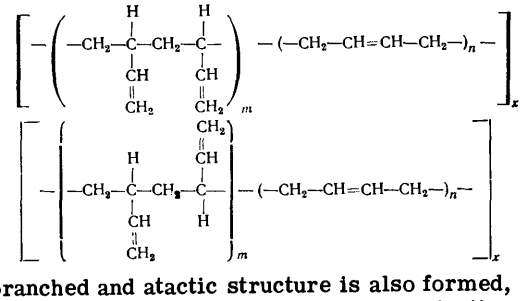
We thus meet a very large variety of abnormal units in the polymers of dienes. The first type of synthetic rubber, obtained by Lebedev's method[20] of polymerising butadiene by the action of metallic sodium, were polymers containing butadiene units linked together at the 1,2- and 1,4-positions in both *cis*- and *trans*-configurations[21]



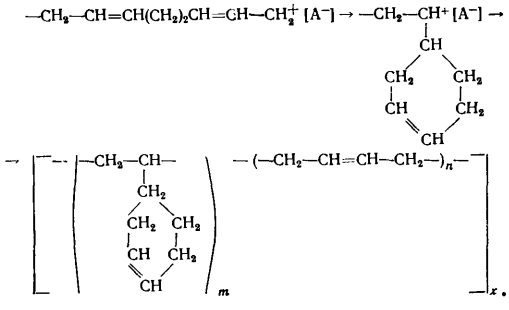
Polymers of butadiene and isoprene obtained in the presence of organometallic catalysts contain far fewer abnormal units. Thus polyisoprene contains 96% and 92% of *cis*-1,4-units when prepared in the presence of a complex of titanium(IV) chloride and triethylaluminium[22] and in the presence of alkyl-lithium catalysts[22,23] respectively. The isoprene polymer obtained in the presence of π-allylnickel iodide contains 95% of 1,4-*trans*-units, 1% of 1,2-units, and 4% of 3,4-units, and its structure can be represented by the formula[24]



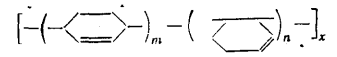
Butadiene and isoprene 1,2-polymers containing predominantly isotactic or syndiotactic units were obtained in the presence of a Ziegler–Natta catalyst[25]. The structure of these heterounit polymers can probably be represented



A branched and atactic structure is also formed, though to a less extent, in the case of ionic polymerisation, as we have already seen in the case of low-pressure (high-density) polyethylene. In the cationic polymerisation of butadiene Dolgoplosk et al.[18,26] observed the formation of six-membered rings by the reaction



The polymerisation of cyclohexa-1,3-diene yields polycyclohexene having different degrees of chemical imperfection depending on the nature of the catalyst: in the presence of organometallic and Ziegler catalysts a polymer containing 1,2- and 1,4-units and having the structure[27]

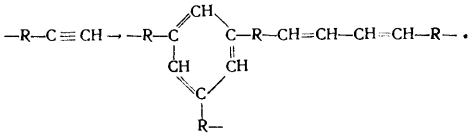


is formed; with π-allylnickel iodide as catalyst the resulting polymer contains 83% of 1,4-units[24].

Atactic polymers, which are formed both in radical and in ionic polymerisation, also represent a case of the presence of randomly arranged foreign *laevo*-units in a chain of *dextro*-units, which is in general characteristic of polymers obtained by radical polymerisation[28]. Natta showed[29] that in this case the difference in structure of the units is stereochemical. Atactic polymers are in general more correctly regarded as random copolymers of *dextro*- and *laevo*-forms, in contrast to a regular copolymer of these forms, represented by the corresponding syndiotactic polymer.

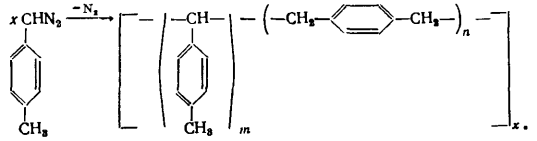
Polymerisation in the presence of oxygen leads to the formation of polymers containing anomalous peroxy-units[30] $CH_2.CHX.O.O$ or ether links $CH_2.CHX.O$ arising from the breakdown of these peroxides. Similar abnormal units appear when polymerisation is initiated by polymeric acyl peroxides, e.g. terephthaloyl peroxide[31]. The initiation of polymerisation by radiation leads to the formation of branched or cross-linked polymers containing abnormal units[32].

In the polycyclotrimerisation of diacetylenic derivatives with the formation of polyphenylenes defective units are produced as residues of incomplete cyclisation[33]:



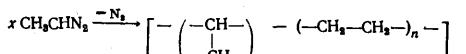
2. Abnormal Units Resulting from Isomerisation of Units During Polymerisation

In several cases of polymerisation the resulting units undergo isomerisation, so that heterounit polymers are formed containing two or more types of units. Isomerisation occurs mostly as a result of hydrogen migration, but cases are known of the migration of chlorine, e.g. in the polymerisation of 3,3,3-trichloropropene, or even rearrangement of the electronic structure of the monomer without the migration of hydrogen, as with acrylonitrile, dimethylketen, glutaraldehyde, and other dialdehydes. Thus Korshak et al. showed[34] that the polymerisation of *p*-tolyldiazomethane involved not only formation of the normal *p*-methylbenzylidene units but also isomerisation with the appearance of an appreciable quantity of *p*-ethylenephenylene units. As a consequence the structure of the resulting polymer corresponds to the formula

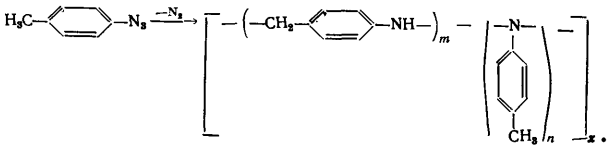


Similar isomerisation was observed in the polymerisation of diazoethane, with the formation of a heterounit polymer

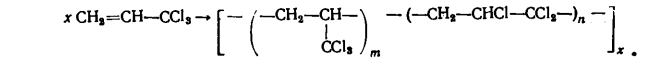
containing ethylene units [35]:



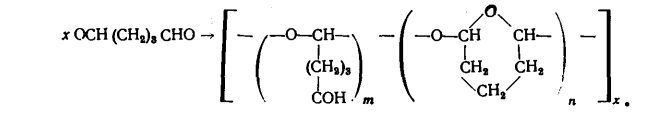
A heterounit polymer with isomerised units probably having the following structure was formed [36] in the catalytic decomposition of *p*-tolyl azide in the presence of sulphuric acid:



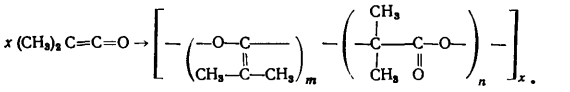
Suprun et al. found [37] that the polymerisation of 3,3,3-trichloropropene, owing to isomerisation involving migration of a chlorine atom, yields a heterounit polymer:



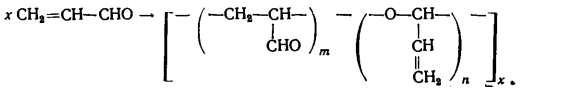
The polymerisation of glutaraldehyde occurs in two ways, with formation of a heterounit polymer [38]:



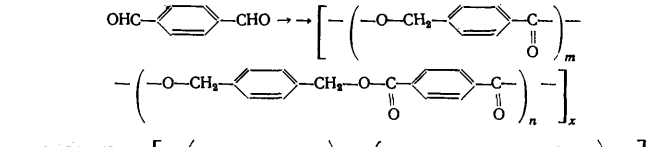
According to Natta et al. [39] dimethylketen polymerises in the presence of triethylaluminium to a polyketone–polyacetal, which is a heterounit polymer:



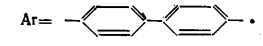
The polymerisation of acrylaldehyde in the presence of weak ionic catalysts lead to the formation of a heterounit polymer containing both ether and carbon–carbon links [40]:



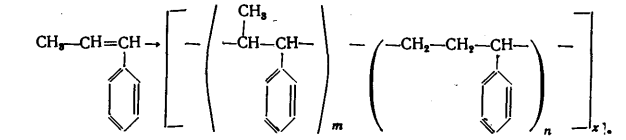
The polymerisation of terephthalaldehyde and of biphenyl-*pp'*-dialdehyde in the presence of organoaluminium or organozinc compounds also shows an unusual course, leading to the formation of heterounit polymers [41,42]:



where

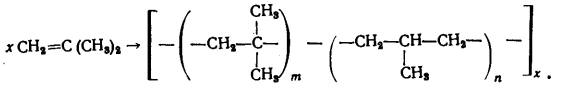


The ionic polymerisation of certain vinyl compounds, substituted styrenes, and vinylpyridines often occurs as migration polymerisation with hydrogen transfer and the formation of heterounit polymers containing in the main chain carbocyclic and heterocyclic rings together with other abnormal units [43,44]. The first case of this type of isomerisation polymerisation with migration of hydrogen [45,46] was probably the polymerisation of anethole [46] and β-methylstyrene [45] studied by Staudinger, which in the latter case gave a heterounit polymer of probable structure

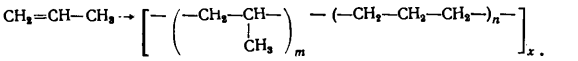


Kennedy showed [48] that an analogous polymer is obtained by the cationic polymerisation of allylbenzene.

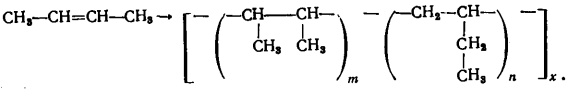
Topchiev et al. [47] showed that in the case of isobutene isomerisation polymerisation led to the formation of a heterounit polymer:



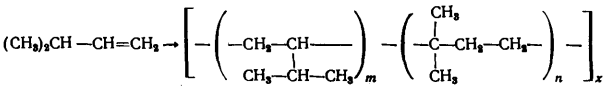
Isomerisation polymerisation with hydrogen transfer has been observed also with many other alkenes [43]. Thus propene gives a heterounit polymer corresponding to a copolymer with ethylene [49,50]:



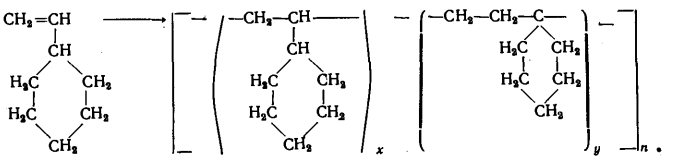
But-2-ene also forms a heterounit polymer [51]:



Isopentene yields a polymer of the following structure [52]:

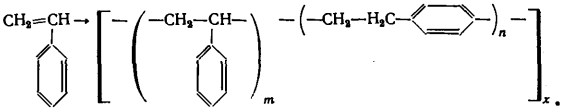


The ionic polymerisation of vinylcyclohexane produces a heterounit polymer containing, together with normal units, abnormal units in which the cyclohexane ring enters the polymer chain [53]:

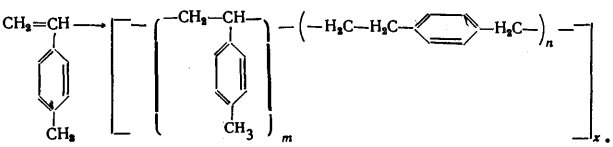


Abnormal monomer units of this type are characteristic of "card" polymers.

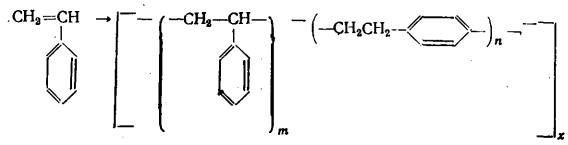
Styrene as a result of isomerisation polymerisation forms a polymer containing not only styrene but also *p*-ethylenephenylene units [54]:



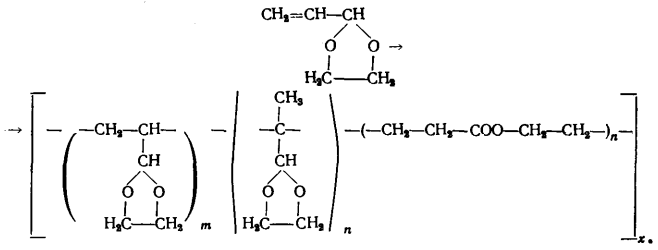
An analogous result was obtained also by the polymerisation of *p*-methylstyrene [55]:



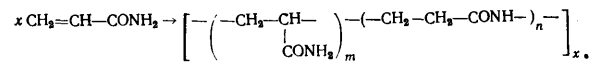
In the case of allylbenzene the resulting polymer has the following structure[56]:



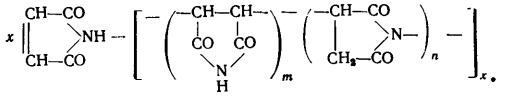
In the case of 2-vinyl-1,3-dioxolan the polymer may have a still more complicated structure[57]:



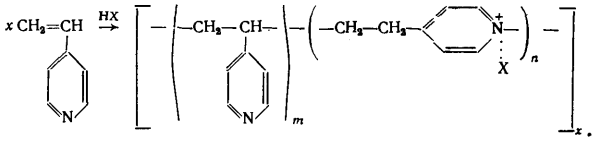
Acrylamide in the presence of basic catalysts undergoes isomerisation to form a heterounit polymer[44,58]:



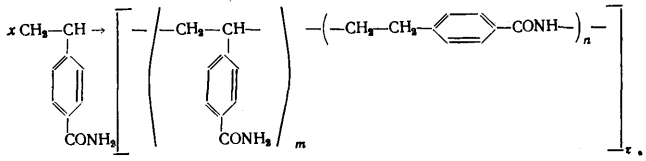
The anionic polymerisation of maleimide in dimethylacetamide similarly yields a heterounit polymer containing not only normal units but also abnormal units formed by the migration of hydrogen[44,59]:



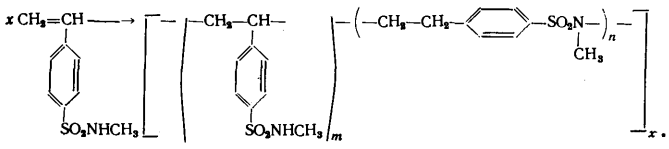
Migration of hydrogen takes place in the polymerisation of 4-vinylpyridine in the presence of acids with the formation of ethylenepyridinium units[60]:



Under conditions of anionic polymerisation *p*-vinylbenzamide forms a heterounit polymer containing different proportions of normal and abnormal units[44,58,59,61-63]:

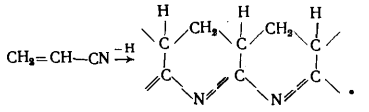


N-Substituted *p*-vinylbenzenesulphonamides behave similarly, forming heterounit polymers by the reaction[44,64,65]



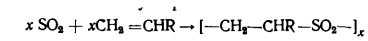
The polymerisation of acrylonitrile under the influence of X-rays[66], γ-rays[67], or fast electrons[68] produces a heterounit polymer containing up to 10% of ketenimine structures:

Nevertheless, the radiation polymerisation of acrylonitrile in the solid phase at low temperatures leads to formation of a syndiotactic polymer, wnereas at high temperatures fused nitrogen-containing rings are obtained[68,69]:

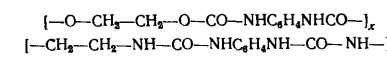


3. Appearance of Abnormal Units during Copolymerisation

Copolymerisation leads to the formation of copolymers containing various quantities and proportions of foreign units, which are therefore heterounit polymers. In this case not only the quantity but also the arrangement of foreign units is especially important. Thus with a regular alternation of the different units we no longer have a copolymer but a true homopolymer having a long repeating unit, as occurs e.g. in the copolymerisation of sulphur dioxide with unsaturated compounds to form polysulphones



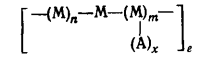
or in the migration copolymerisation of diols or diamines with di-isocyanates to form polyurethanes or polyureas



The concept of the defectiveness of macromolecules is of practical value, of course, only when one type of unit predominates. When the two types of units are present in equal quantities, the concept obviously loses the meaning in which it is used in the present paper.

Simultaneous polymerisation may lead to the formation of different types of copolymers, which may even have the same elementary composition. Thus at present we are acquainted with such different types as block copolymers (in particular polyallomers), graft copolymers, random copolymers, and also diagonal or insymmetrical copolymers and copolymers with a regular alternation of different units[70-72]. The introduction of one or more other types of copolymers into a particular type will undoubtedly yield a "copolymer of copolymers", which may be a polymer with chemically defective macromolecules.

Among the above types of copolymers those with a regular alternation of units must be regarded as homopolymers. Their structure can be represented by the general formula $[M.A]_x$, whereas in the case of statistical copolymers, which are heterounit polymers, the general formula expressing their structure will be $[[M]_n.[A]_m]_x$, where $n = 1, 2, 3, \ldots$, $m = 1, 2, 3, \ldots$, and $n \neq m$. Hence we should again have a regular copolymer when $n = m$. A block copolymer will be represented by the same general formula but with $n \neq m$, $n > 10$, and $m > 10$. In the case of a graft copolymer the general formula will be



in which $n + m > 1000$, $x > 10$, and $e = 1-10$ and above.

The copolymerisation of styrene with divinylbenzene by Staudinger [73] was the first case in which a branched and cross-linked polymer was obtained. This type of imperfection is met widely in ion-exchange resins, since in this way insoluble granules of limited swelling can be obtained. The "copolymerisation" of styrene with ϵ-caprolactam also yields a graft copolymer with a chemically imperfect macromolecular structure [74].

The peculiar polymers known as "diagonal" or "unsymmetrical", obtained by the copolymerisation of a mixture of two monomers of variable composition, should also be regarded as heterounit polymers. They differ from the other examples in the variation in structure of the units along the length of the macromolecule [71].

A more detailed description of copolymerisation and the properties of copolymers lies outside the scope of the present paper. The account will therefore be confined to the above examples, illustrating the fact that most copolymers are heterounit polymers.

4. Formation of Abnormal Units during Polycondensation

Two groups of polycondensation processes, differing significantly in reaction mechanism and termed respectively "equilibrium" and "non-equilibrium" polycondensation, have been distinguished. We must therefore take into account their differences in considering individual examples of reactions of each type [75-83]. Heterounit polymers can also be formed in various ways during polycondensation.

As in the various cases of polymerisation discussed earlier, polycondensation may also involve reactions leading to the formation of various abnormal units—containing side-chains and branches, cross-links, anomalous groups in the main chain—as well as all kinds of stereochemically distinguishable units yielding macromolecules having structures similar to those in atactic, isotactic, and syndiotactic polymers obtained by stereospecific polymerisation. The concept of "tacticity" has a specific sense when applied to polycondensates [84]: it covers units containing carbon atoms with two different substituents, *cis*- and *trans*-isomers with multiple bonds and with a disubstituted ring, and also groups with central, axial, and planar asymmetry. In complicated polymers stereoregular structures may be formed also as a result of the appearance of stable conformations [85]. Another important source of abnormal units is the residue of incompletely cyclised units remaining during polycyclisation or polycyclocondensation.

Let us cite a few examples of the formation of heterounit polymers during equilibrium polycondensation. Thus the polycondensation of dicarboxylic acids with glycols in the presence of mineral acids is accompanied by the formation of ethers:

$$HOR—OH+HO—R—OH \xrightarrow{-H_2O} HO—R—O—R—OH.$$

As a consequence, abnormal units containing an ether bond

$$—O—R—O—R—O—CO—R'—CO—$$

appear in the polyester macromolecule [86]. In the polycondensation of glycerol this reaction leads to the formation of units containing biglycerol

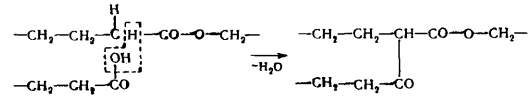
$$—O—CH_2—\underset{\displaystyle OH}{CH}—CH_2—O—CH_2—\underset{\displaystyle OH}{CH}—CH_2—O—$$

and polyglycerols [87,88].

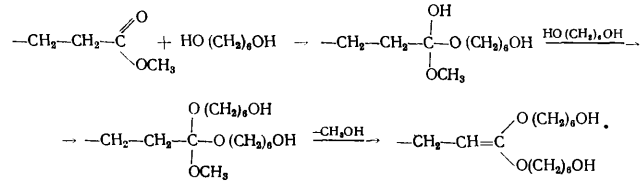
The equilibrium polycondensation of ethylene glycol with terephthalic acid or its dimethyl ester in the presence of most catalysts leads to the formation of poly(ethylene terephthalate) melting at 256°C. [89] However, the use of sulphuric acid as catalyst yields a polyester of lower melting point, owing to the formation of a heterounit polymer containing ether bonds

$$[—(—OCH_2CH_2OCOC_6H_4CO—)_m—(—OCH_2CH_2OCH_2CH_2OCOC_6H_4CO—)_n—]_x.$$

The formation of branched polyesters on prolonged heating of the reaction mass was observed by Staudinger and Schmidt [90], who explained this result by dehydration



or by formation of a keten acetal



When unsaturated monomers such as maleic and fumaric acids are used in polycondensation, polyesterification is accompanied by secondary addition of the glycol to the double bond with the formation of hydroxyethoxysuccinic esters [91,92]:

$$—CO—CH=CH—CO—O—CH_2CH_2—O— \xrightarrow{HOCH_2CH_2OH} \rightarrow —CO—CH_2—\underset{\displaystyle O—CH_2—CH_2—OH}{CH}—CO—O—CH_2CH_2—O—.$$

At the later stages of conversion this reaction leads to branching and cross-linking of the polymer. During polycondensation with the glycols investigated in detail by Petrov [93] and by others [94] maleic acid isomerises into fumaric acid, to yield polyesters which are heterounit polymers, and can be regarded also as copolymers of the two acids. The degree of conversion may reach 70–90% depending both on the nature of the glycol and on the conditions of polycondensation.

Polyamides prepared by prolonged heating in the molten state form branched products having the structure

$$\begin{matrix}—NH(CH_2)_6NH—CO(CH_2)_8CO \\ —NH(CH_2)_6NH—CO(CH_2)_8CO\end{matrix}\!\!>\!N(CH_2)_6NH—CO(CH_2)_8CO—.$$

Such observations were made by Champetier [95,96] and by other workers [97-99] on both aliphatic and aromatic polyamides. According to Meacock [100] as well as Kamerbeek et al. [101] heterounit polyamides result from the formation of secondary amino-groups by the reaction

$$—CO(CH_2)_4CO—NH(CH_2)_6NH_2 + H_2N(CH_2)_6NH—CO(CH_2)_4CO— \xrightarrow{-NH_3} \rightarrow —CO(CH_2)_4CO—NH(CH_2)_6NH(CH_2)_6NH—CO(CH_2)_8CO—.$$

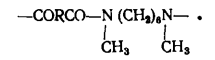
These groups react with terminal carboxy-groups of other macromolecules to produce branched polyamides

$$—CO(CH_2)_4CO—NH(CH_2)_6\underset{\displaystyle CO(CH_2)_4CO—NH(CH_2)_6NH—}{N}(CH_2)_6NH—CO(CH_2)_4CO—.$$

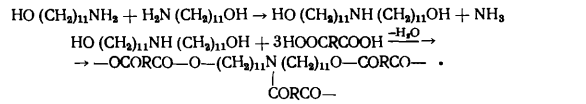
Thomas showed [102] that, when polyamides are prepared from diamines and dicarboxylic esters at high temperatures, the diamine may undergo alkylation

$$H_2NRNH_2 + 2R'COOCH_3 \rightarrow CH_3NHRNHCH_3 + 2R'CO[illegible]$$

with the formation of methyl side-groups in the polyamide

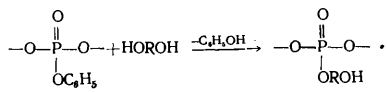


The formation of branched and three-dimensional poly(amide–esters) by the polycondensation of ω-amino-alcohols with dicarboxylic acids results from the elimination of ammonia and the formation of amino-glycols [103]:



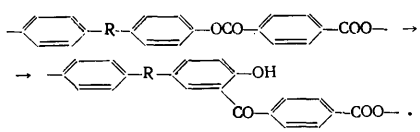
The presence of different functional groups in the initial monomers, and subsequently in the polymer macromolecule, may lead to branching and ultimately to the formation of three-dimensional polymers, as has been shown with *N*-cyanoethylated polyamides [104].

The synthesis of poly(ethyl ethylene orthophosphates) is accompanied by transesterification with the formation of branches [105]:

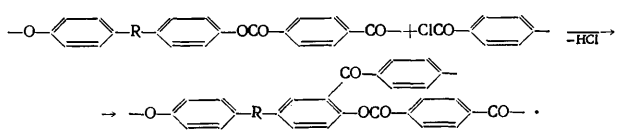


Formation of branched polyesters in the polycondensation of a glycol with an unsaturated acid, e.g. fumaric or maleic, may result also from the dimerisation or the polymerisation of the acid during the reaction [106]. Lavalou [107] observed cross-linking also in the polycondensation of ω-aminoundecanoic acids containing such *N*-substituents as allyl, undec-10′-enyl, and 2′-hydroxyethyl. Cross-linking of polyesters may result also from their oxidation by oxygen during preparation [108].

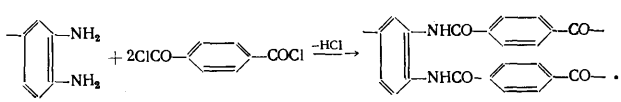
Although the laws of non-equilibrium polycondensation, like the structure of the polymers obtained, have been investigated less thoroughly, we shall consider some examples showing that heterounit polymers are formed in this process. Branched polymers may be produced by direct acylation or by a rearrangement analogous to the Fries rearrangement. Thus in the synthesis of polyarenoates branching may occur in conformity with the equation [109]



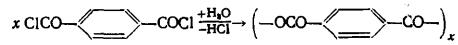
The resulting phenolic hydroxyl in then able to react with an acid chloride to form a branch. Acylation can cause branching as a result of the reaction



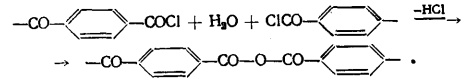
Branching can occur in the reactions of the dichlorides of dicarboxylic acids with tetramines, bis-*o*-amino-phenols, and bis-*o*-amino-thiols:



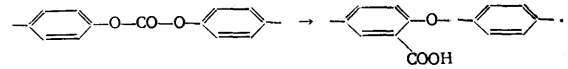
The action of water on a solution of such a dichloride in triethylamine yields a polyanhydride of terephthalic acid [110]:



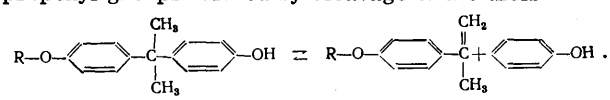
Therefore the presence of traces of moisture in the low-temperature polycondensation of acid chlorides with dihydric phenols may lead to the appearance of anhydride groups in the macromolecule by the reaction



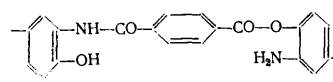
Schnell [111] considered it possible that a Kolbe type of side-reaction leading to the formation of branched and cross-linked structures may occur in the preparation of polycarbonates from diphenyl carbonate:



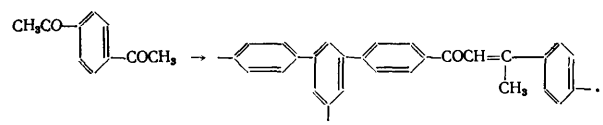
He also considers [112] that branching may result from the polymerisation of polycarbonates involving terminal isopropenyl groups formed by cleavage of the diols



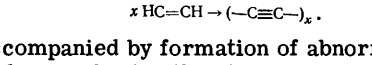
When dichlorides of dicarboxylic acids undergo polycondensation with biaminophenylmethanediols or bisaminophenylmethanedithiols (in which the amino-group is *ortho* to the hydroxy- or mercapto-group), their analogues and homologues, reaction can occur in two directions with the formation of abnormal units of isomeric structure, e.g.



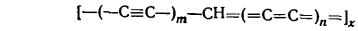
In the polycyclocondensation of diketones the phenyl rings may be accompanied by aliphatic units remaining from incomplete cyclisation [113]:



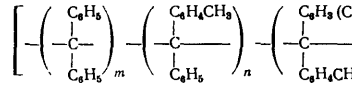
The oxidative dehydropolycondensation of acetylene yields a linear form of polymeric carbon, which is a third allotropic modification of carbon termed "carbyne" [114]:



This is accompanied by formation of abnormal units and block copolymers having the structure



A side-reaction in the polyrecombination of diphenylmethane is methylation of the benzene rings by the action of methyl radicals, so that the resulting polymer contains tolyl and xylyl groups [115]



Polycyclisation is one of the most important types of reactions in non-equilibrium polycondensation [116]. It occurs in two stages: the linear polymer formed initially then undergoes cyclisation, and is thus converted into a

ring–chain polymer. However, several examples have shown that the second stage is almost always incomplete. One reason is increasing rigidity of the chain causing steric hindrance to cyclisation. This is shown in an increase in the activation energy of cyclisation during the process, as illustrated by Fig. 2, in which are plotted results of the cyclisation of a polyhydrazide [117]. The reason for this increase in activation energy and consequent decrease in rate of polycyclisation is the stiffening of the polymer macromolecules caused by the formation of oxadiazole rings, since this diminishes the mobility of the units necessary for them to overcome the stereochemical obstacles to cyclisation. Therefore the macromolecules of the resulting ring–chain polymer always retain some proportion of uncyclised units as a residue of incomplete cyclisation: i.e. these are abnormal units in the resulting heterounit polymer.

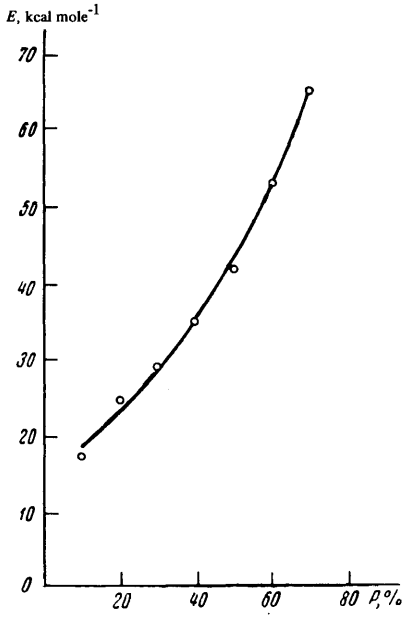
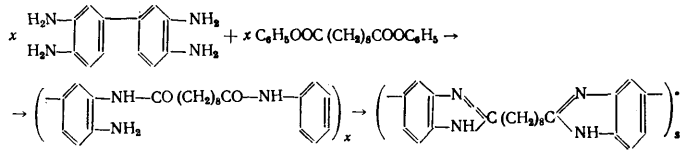
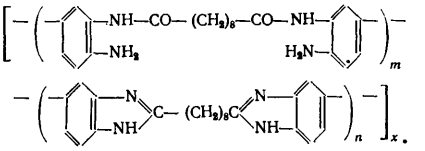


Figure 2. Variation of activation energy for the cyclodehydration of a polyhydrazide of diphenylphthalidedicarboxylic acid with completeness of conversion P.

Thus the polycondensation of aromatic bis-*o*-diamines with diphenyl esters of aromatic dicarboxylic acids leads to the formation of polybenzimidazoles:

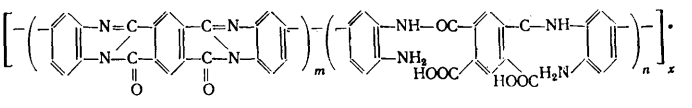


At any stage in this reaction, however, the product is a heterounit polymer containing amino-amide and benzimidazole units in the macromolecule, so that its structure is more correctly represented by the formula [118,121,122]

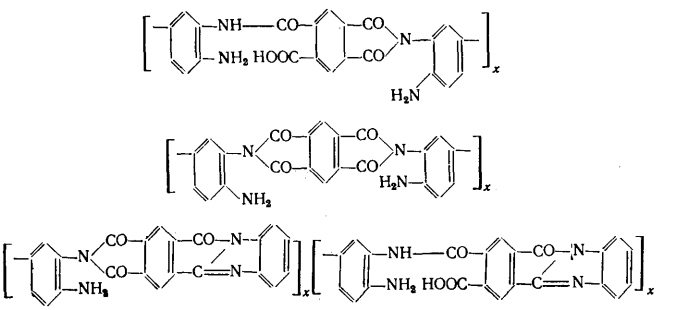


Examination of polybenzimidazoles which have been dehydrated at 270°C showed that they contained about 69% of benzimidazole and 31% of amino-amide units [121].

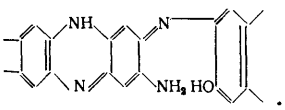
The structure of pyrrones—products of the reaction between tetracarboxylic anhydrides and bis-*o*-diamines—has also been studied very carefully in view of the especially high thermal stability expected [123–129]. Application of a thermodynamic method by Rabinovich et al. [123] established that the pyrrone macromolecule contains 66% of benzoylenebenzimidazole and 34% of amino-amide units, the latter remaining from incomplete cyclisation. Their structure is therefore represented more accurately by the formula



It must be borne in mind, of course, that this formula contains only the two extreme structures: several intermediate structures may also be present, formed in the passage from the amido-amino-acid to the benzoylenebenzimidazole, e.g.



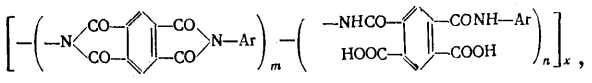
Incomplete cyclisation has also been suggested in the ladderlike polyquinoxalines obtained by Stille and Mainen [130] from 2,5-dihydroxy-*p*-benzoquinone and benzene-1,2,4,5-tetra-amine, so that the chain should contain units of the two types



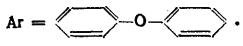
A similar hypothesis was put forward by Okeda and Marvel for polyquinoxalino-oxazines [131] and polyquinoxalino-thiazines [132].

Polypyromellitimides also contain a considerable quantity of uncyclised units. Thus Bruck [133] found that the polypyromellitimide obtained from bis-*p*-amin[illegible]yl ether contained only 78% of imide units, with 22% of

amido-acid units remaining uncyclised, so that a more correct formula for this heterounit polymer is



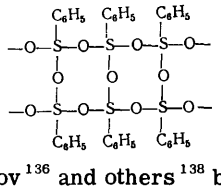
where



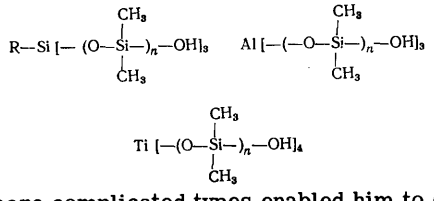
Investigation of several polyheteroarylenes obtained recently has revealed the presence of a considerable quantity of uncyclised units also in polyquinoxalines [130], polybenzoxazoles [134], polyoxadiazoles [117], polypyridines [135], etc.

Thermal dehydrocyclisation—a process widely applied to the synthesis of various thermostable polymers—represents a novel type of pyrolysis involving the elimination only of water. Genuine pyrolysis is often a polycondensation process occurring with the elimination of volatile products—water, carbon dioxide, carbon monoxide, hydrogen, methane and other saturated and unsaturated hydrocarbons, and benzene and other aromatic compounds—the composition of which varies with the temperature and the conditions of pyrolysis. The non-volatile product of pyrolysis is coke or graphite, whose structure and properties also depend on the structure of the starting materials and the conditions of pyrolysis.

The polycondensation of monomers containing three or more functions leads to the formation of branched and cross-linked polymers containing abnormal units. Andrianov [136,137] showed with several polymers that the functionality and the structure of the initial monomers play a very important role. Thus a three-dimensional polymer with a regular arrangement of rings can be obtained [137] by the polycondensation of cruciform polytitano-organosiloxane oligomers. An especially detailed investigated was made of the ladderlike polymer of structure

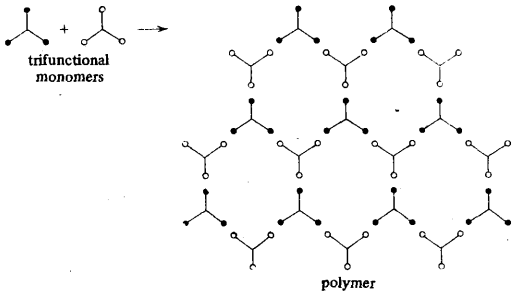


obtained by Andrianov [136] and others [138] by the hydrolysis of phenyltrichlorosilane. Its macromolecule contains defects consisting in incomplete ring closure [139]. In the case of three-dimensional polymers it is very important to ensure maximum regularity of the network structure, which is achieved by using tri- and tetra-functional oligomers having the same side-chains [137]. Thus Andrianov's use of oligomers of the type



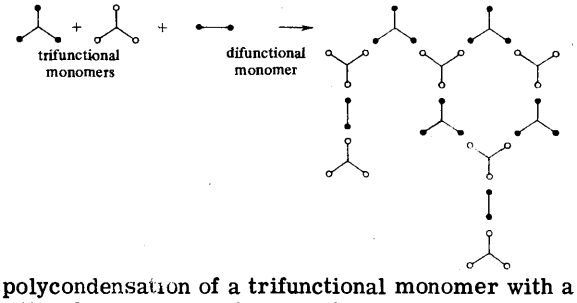
and also more complicated types enabled him to obtain polymers having a regular network structure [137].

Defects of two kinds—rings (loops) and long side-chains attached at only one end to branch points of the network—may appear on formation of a network structure [140]. The structure of the initial substances is evidently of especial importance. Thus an extremely regular network could probably be obtained by the polycondensation of two trifunctional monomers [141]:

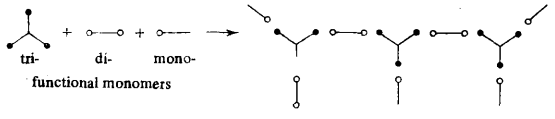


In the work cited above Andrianov proved experimentally the possibility of obtaining such regular structures [136,137].

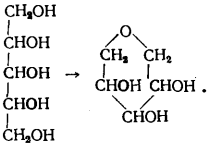
The regularity of the three-dimensional framework undoubtedly breaks down in the polycondensation of trifunctional with difunctional and especially with monofunctional monomers, which makes such a system chemically imperfect owing to the appearance of many abnormal units, as shown below. The picture for the polycondensation of trifunctional monomers when one of them has been replaced by a difunctional monomer will be



The polycondensation of a trifunctional monomer with a difunctional monomer and a monofunctional monomer can be depicted



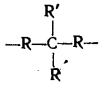
The polycondensation of polyhydric alcohols with dicarboxylic acids will be accompanied by the side-reactions considered above, together with substitution, cyclisation, etc. leading to the formation of abnormal units [142]. An interesting case of the formation of heterounit polymers was observed by Kiselev and Lubman [143] in the polycondensation of xylitol with phthalic anhydride, when abnormal units resulted from secondary dehydration with the formation of cyclic ethers:



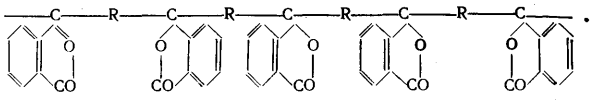
Most polymers obtained by polycondensation methods contain symmetrical units, so that the stereoregularity of their structure does not attract the attention of investigators. As with polymerisation methods, however, it must be envisaged that stereoregular polymers can be prepared by polycondensation. The first necessary condition for achieving this aim is, of course, the use of polymers capable of forming asymmetric units. This has already

been realised in practice by starting with optically active monomers, which enable polymers to be obtained with a sterically regular alternation of units.

Use is generally made of monomers having two different and two identical substituents of the type

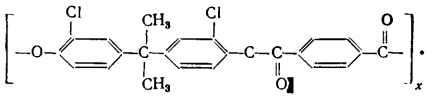


but this yields polymers having a structure analogous to that of atactic polymers, i.e. with sterically non-equivalent units. Consequently these units can also be regarded as abnormal relative to each other, and such polymers as heterounit. An example of this type is supplied by the "atactic" polyarenoates of phenolphthalein and various dicarboxylic acids, which have the schematic formula

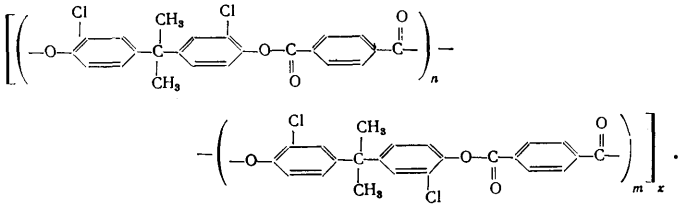


As we shall see later, this view of its structure is supported by its physical properties [144].

When bulky substituents are present, polyarenoates are produced having different crystal forms depending on the nature of the solvent. Thus the polyarenoate of 2,2-bis-*m*-chloro-*p*-hydroxyphenylpropane and terephthalic acid obtained in the presence of pyridine is crystalline and gives narrow signals in the nuclear quadrupole resonance spectrum, indicating the predominance of one crystalline form [85], so that this polymer can be regarded as stereoregular. It probably has the structure



When this reaction is conducted in dioxan and other solvents, a heterounit polymer is formed containing both crystallographic conformations, which can be represented by the formula



Thus this reaction is an example of the synthesis of a stereoregular polymer by stereospecific polycondensation.

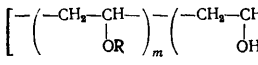
5. Appearance of Abnormal Units during Copolycondensation

Copolycondensation, like copolymerisation, results in the formation of "heterounit polymers" containing units differing in structure. Polymers having macromolecules of varying degrees of imperfection are obtained depending on the nature and the quantity of the monomers taken. The use of monomers having three or more functions enables polymers to be obtained containing substituent groups and side-chains, as well as cross-linked three-dimensional structure. A more detailed description of the structure of the copolymers obtained is outside the scope of the present paper, so that reference will be made to the monograph on this topic [75].

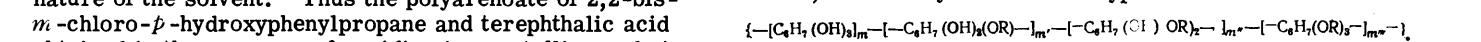
6. Formation of Various Abnormal Units during the Substitution, Oxidation, and other Reactions of Macromolecules

Heterounit polymers can be obtained also as a result of substitution in the macromolecule of hydroxy-groups, hydrogen atoms, halogen atoms, and other atoms or groups by halogenation, oxidation, metallation, and other reactions. Since such reactions never go to completion, a heterounit polymer is obtained containing the initial units, together with the final and intermediate substitution products. The distribution of substituents resulting from substitution is usually random.

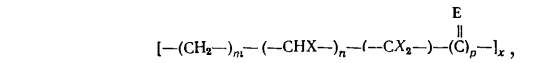
An extremely clear example of reactions of this kind is the polymerlike substitution in the hydroxy-groups of cellulose, polyvinyl alcohol, starch, and other polymers containing easily replaceable hydrogen atoms, which are usually only partly replaced by various groups. As a result of this, polyvinyl alcohol forms a heterounit polymer having the structure [145]



A still more complicated situation is found in cellulose ethers, which may contain four types of units [146]

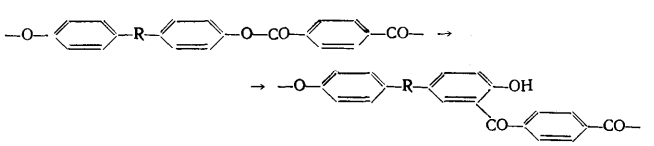


The same consideration applies to the huge number of heterounit polymers of various types, whose chains may contain two, three, or more different units in various proportions. They include both copolymers obtained by the copolymerisation of different monomers, which we have discussed previously, and heterounit polymers formed by the replacement in a homopolymer of hydrogen or other atoms or even whole groups as a consequence of such reactions as oxidation, chlorination, hydrochlorination, dehydrochlorination, esterification, alkylation, acylation, sulphonation, nitration, metallation, etc. These reactions yield heterounit polymers containing, together with the original monomer units, irregularly arranged mono- and di-substituted units, which can be represented for a substituted polyethylene by

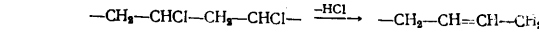


where X = Cl, Br, I, F and E = O, S.

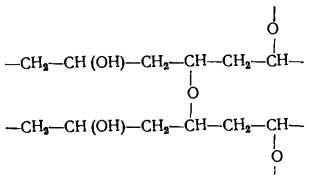
Abnormal units and consequent chemical imperfection may result also from various reactions leading to the formation of heterounit polymers—the Fries rearrangement in polyarenoates, the elimination of hydrogen chloride from poly(vinyl chloride) and other halogenated polymers, the removal of water from polyvinyl alcohol and from polymethacrylic acid, etc. The Fries rearrangement



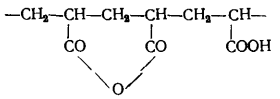
takes place when polyarenoates are exposed to ultraviolet radiation or are treated with aprotic acids [147]. The elimination of a hydrogen halide from halogenated polymers results in the appearance of double bonds [148,149]:



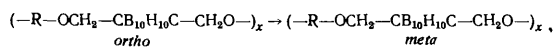
Dehydration of polyvinyl alcohol leads to cross-linking by ether bonds



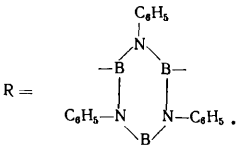
and the polymer becomes insoluble [150]. Elimination of water from polymethacrylic acid converts it into the cyclic anhydride [151]



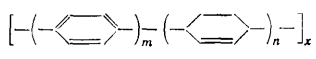
An interesting and very peculiar case of the formation of a heterounit polymer is the isomerisation of polyethers containing bishydroxymethyl-*o*-carborane residues into polyethers of bishydroxymethyl-*m*-carborane, which occurs on prolonged heating in an inert atmosphere [152]:



where

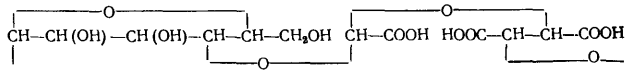


Marvel's synthesis of polyphenylene [27] involves a stage of polymerisation of cyclohexa-1,3-diene followed by dehydrogenation of the resulting polycyclohexene. The latter reaction is incomplete, so that actually the product is not poly-*p*-phenylene but the heterounit polymer

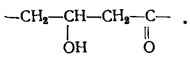


containing phenylene and cyclohexene units.

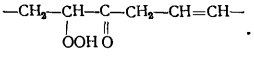
The oxidation of polymers results in the formation of heterounit polymers whose macromolecules contain carboxyl, ketone, alcohol, and other groups formed by oxidation of a monomer unit. Thus oxidised cellulose



comprises [146] units containing carboxy-groups formed both by oxidation of terminal primary alcohol groups and by cleavage of a pyran ring. Marvel and Denoon [153] showed that oxidised polyvinyl alcohol contains keto-groups



Oxidised polyethylene contains peroxy- and keto-groups together with double bonds [154]:



Nearly every polymer is oxidised on standing in air for a long time, and therefore contains aldehyde and ketonic groups, carboxyls, and peroxy-groups [155].

Marvel and Sampel [156] showed that dehydrochlorination of poly(vinyl chloride) leads to the formation of double bonds in the chain and the appearance of a dark colour in the polymer [156].

An immense number of heterochain polymers of varying structure—e.g. polyamides, polyesters, poly(amide–esters), etc.—have quite polar bonds in their chain, and therefore readily undergo exchange reactions with analogous heterochain polymers to form heterounit polymers. The products have the same structure and properties as copolymers synthesised from the corresponding initial monomers [157].

Heating a mixture of polyhexamethylenedipamide and poly-6-hexanoamide yields mixed polyamides having the same properties as those obtained by the reaction of hexamethylenediammonium adipate with ϵ-caprolactam [97]. In the same way, heating a mixture of three polyamides—polyhexamethylenedipamide, polyhexamethyleneazelaamide, and poly-ϵ-caproamide—results in a mixed polyamide with the properties of the polymer obtained by polycondensation of the corresponding starting materials [157]. When a mixture of two polyesters is heated, a heterounit polymer is formed with the same properties as in the corresponding copolymer obtained from the initial monomers [158,159]. Similarly, a poly(amide–ester) was obtained by heating a mixture of a polyamide and a polyester [160].

Another interesting feature of exchange reactions between two heterochain polymers is that, together with the statistical copolymer which is the final result of such a process, block copolymers appear in the early stages [97]. We obtain a mixture of various copolymers with abnormal units depending on the stage at which the reaction is halted, as shown in Fig. 3.

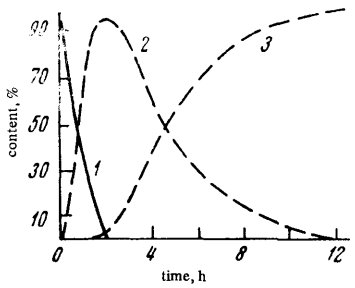
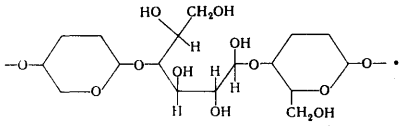


Figure 3. Variation in composition of a mixture of two heterochain polymers during heating: 1) homopolymers; 2) block copolymers; 3) random copolymer.

The formation of cross-linked polymers by various types of vulcanising reactions also produces chemically defective macromolecules [73,161,162]. Thus polyethylene, when heated with a peroxide [161], exposed to radiation [162], or treated with other chemical reagents becomes initially branched, and then an insoluble, infusible, cross-linked three-dimensional product. This type of imperfection resulting from chemical or radiation treatments occurs in many polymers, and is widely used in technology. The network produced in vulcanising and similar cross-linking processes is in most cases irregular, and usually results in chemically defective heterounit polymers.

7. Natural Polymers containing Abnormal Units

The examples we have been considering have been drawn mainly from synthetic polymers. In conclusion, therefore, we will cite examples of chemically imperfect macromolecules in natural polymers. Pacsu [163] and Strepikheev [164] showed that such an important natural polymer as cellulose contains, together with cyclic units, abnormal, acyclic units, as in the formula



Natural rubber contains 97–98% of *cis*-1,4-units and a small quantity (2–3%) of *trans*-units with units of different structure [22]. Deoxyribonucoeic acid, which plays such an outstanding part in the transmission of inherited characters, can also contain abnormal units in the chain, whose presence leads to the appearance of mutations and inherited diseases [165,166]. Thus abnormal units appear in appreciable quantities even in the synthesis of polymers in living organisms.

The above examples show that almost all known methods for synthesising and modifying polymers result in the formation of compounds that are heterounit polymers and contain chemically defective macromolecules. In practice, therefore, we are always dealing with heterounit polymers whose macromolecules contain abnormal units.

III. EFFECT OF ANOMALOUS MONOMER UNITS ON CHEMICAL PROPERTIES OF HETEROUNIT POLYMERS

The presence of abnormal units in the chain of a heterounit polymer should undoubtedly have a significant influence on the whole complex of its inherent chemical and physical properties. Primary importance will, of course, attach to the nature and number of abnormal units and their arrangement in the polymer chain. Very little information is yet available which could clearly illustrate the details of such effects, but the general picture has become quite distinct.

Let us consider individual examples of how the chemical properties of a polymer may vary under the influence of abnormal units. The differences between the chemical properties of heterounit polymers and those of the ideal polymer containing only one type of unit, taken as the initial standard for comparison, is larger the more the abnormal units differ from the main units constituting the macromolecule. Thus the formation of a branch in the radical polymerisation of vinyl compounds leads to the appearance in the macromolecule of units containing tertiary hydrogen atoms and side-chains, which are anomalous for this structure. The consequence is diminished resistance to oxidation, since tertiary hydrogen atoms are oxidised very easily, and therefore become points from which chain oxidation reactions begin, leading to degradation of the polymer [167].

Investigation has in fact shown that the thermal degradation of branched polyethylenes is initially considerably more rapid than that of the linear polymers (Fig. 4) [168]: only at 60% breakdown of the polymer do the rates of degradation of the two polyethylenes become equal. It is interesting that the rate of degradation of branched polyethylenes increases with increase in the degree of branching, i.e. in the content of side-chains, as is evident from Fig. 5. [169] Similarly, the branching of polymers containing aromatic rings diminishes their thermal stability, since benzene rings containing three substituents are more easily oxidised, being weak spots in the macromolecule.

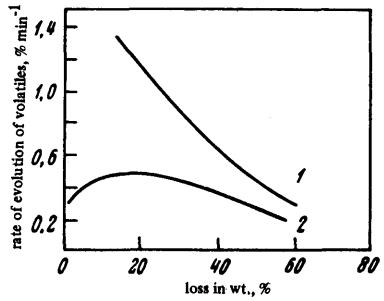


Figure 4. Rate of evolution of volatile products during the heating at 400°C of polyethylene: 1) branched; 2) linear.

The presence of monomer units linked "head to head" in vinyl polymers results in the appearance of anomalous groupings containing adjacent halogen atoms or hydroxy-groups, as e.g. in poly(vinyl chloride) or polyvinyl alcohol [153]



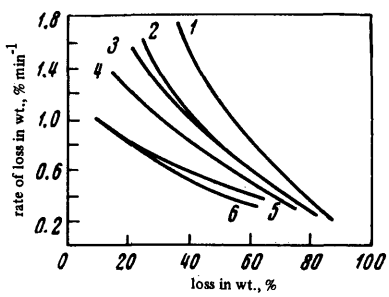
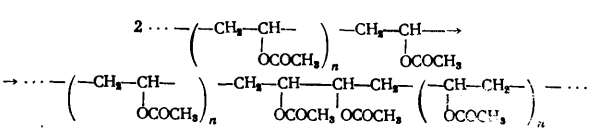
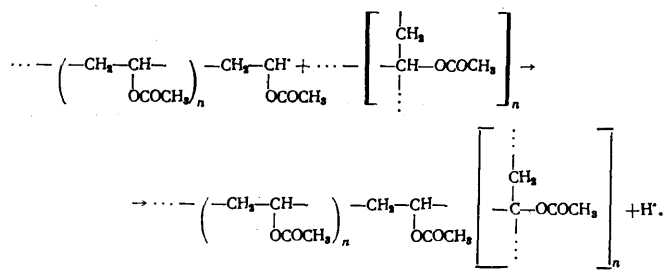


Figure 5. Rate of loss in weight at 400°C for specimens of branched, high-pressure polyethylene having different contents of side-groups (CH_3 per 100 CH_2): 1) 8.7; 2) 6.9; 3) 6.0; 4) 5.6; 5) 3.9; 6) 3.7.

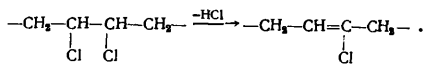
The latter polymer is found to contain ~1% of 1,2-groupings [170], which differ in chemical properties from 1,3-groupings typical of these polymers [153,170]. Such 1,2-groupings may be formed [170] as a result both of the recombination of macroradicals



and of chain transfer



The effect of such anomalous units was shown very clearly in an investigation of the thermal stability of two polymers of vinyl chloride and of vinylidene chloride, in which the units were arranged "head to head" and "head to tail" [171]. Fig. 6 shows that decomposition was slower in the former than in the latter case. The explanation is that, although the first stage in the reaction is more rapid for a "head to head" polymer, it leads to the formation of a stable structure resembling chloroprene, by the reaction



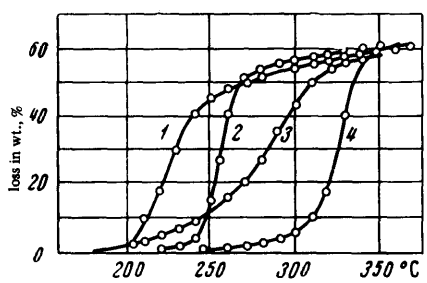
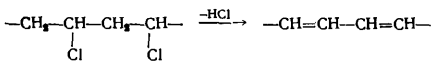


Figure 6. Thermal breakdown of:
1) "head to tail" poly(vinylidene chloride);
2) "head to tail" poly(vinyl chloride);
3) "head to head" poly(vinyl chloride;
4) "head to head" poly(vinylidene chloride).

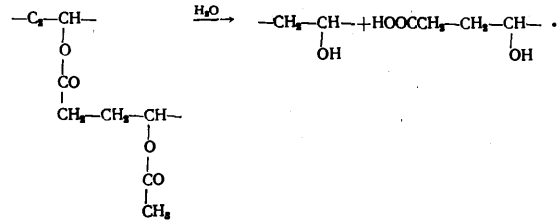
Chain dehydrochlorination is therefore unable to develop further along the macromolecule. In a "head to tail" structure, however, dehydrochlorination



proceeds along the chain until complete. Nevertheless, if abnormal units containing chlorine atoms in the 1,2-positions are present in such a chain, dehydrochlorination will be interrupted.

Examination of poly(vinylidene fluoride) by nuclear magnetic resonance spectroscopy showed that the content of units linked "head to head" varied between 8.6% and 10.6%. [172]

The presence of abnormal units in poly(vinyl acetate) (Section II, 1) results in a decrease in molecular weight on hydrolysis, owing to saponification of the ester bonds [17]:



The polymers of methyl α-chloroacrylate and α-bromoacrylate contain predominantly monomer units linked "head to head" [173]. Monomer units are assumed to be linked in different ways also in polystyrene [54].

Stereochemical relations in the structure of the units in polysaccharides influence their chemical properties especially strongly. Thus natural cellulose and its modification containing 3,6-anhydroglucose as well as glucose units differ in their liability to acid hydrolysis, which according to Rogovin et al. [174] is appreciably lower in cellulose. Similarly, the acetylation of cellulose is slower than that of modified cellulose containing altropyranose units [175]. The presence of anomalous groupings in the cellulose macromolecule, which are more easily hydrolysed than the principal units, facilitates its degradation on hydrolysis, as was shown by Pacsu [163] and by Strepikheev [164]. The increased rate of hydrolysis of cellulose in the first stage is explained by the fact that the abnormal units are "open" structures (Section II, 7), which are less resistant than cyclic structures to acid hydrolysis.

The chemical imperfection of the macromolecules of atactic polymers is shown also in a marked difference in rates of reaction from those of stereoregular polymers [176]. The temperatures at which half the weight of the polymer is lost on heating for 35 min (including heating to this temperature in 15 min) are 295° and 312°C for atactic and isotactic poly(propylene oxide) respectively, and the corresponding activation energies are 20 and 45 kcal mole^{-1}. [176] Similarly, atactic and isotactic polystyrene have activation energies for pyrolysis of 24.5 and 42 kcal mole^{-1}. [177]

The temperature characteristics—primarily the thermal stability—are among the most important indications of the chemical stability of a polymeric structure. The presence of defective units resulting from incomplete cyclisation diminishes the thermal stability of polymers [1,2]. Fig. 7 illustrates the results of a dynamic thermogravimetric analysis showing that a pyrrone is more thermostable than the corresponding poly(amide–aminoacid). However, the observed difference may depend on the dominant importance of dehydration in the acid. Fig. 8 therefore shows the quantities of water and carbon dioxide evolved at various temperatures. Differences are observed not only for water but also for carbon dioxide [127]. Evolution of the latter from the polymeric acid not only begins at a lower temperature than in the case of the pyrrone (200° and 300°C) but also occurs in far larger quantity. It can thus be accepted that defectiveness of the polymer structure consisting of the presence of abnormal units is one cause of the diminution in the thermal stability of polymers [1,127,178].

Polyphenylene, obtained by Marvel's method [27] of dehydrogenating poly-1,4-cyclohexene, has low thermal stability, which is explained by the presence of incompletely aromatised cyclohexene units in its macromolecules.

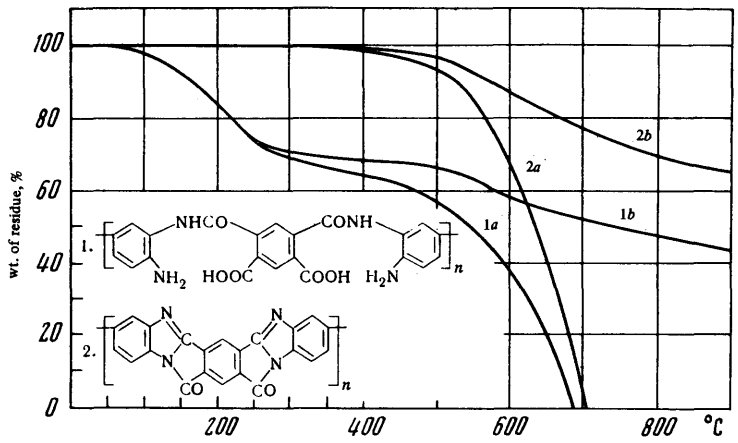


Figure 7. Dynamic thermogravimetric analysis (rate of heating 5 deg min^{-1}) of:
1*a*) poly(amide–amino acid) in air; 1*b*) poly(amide–amino acid) in helium;
2*a*) polybenzoylenebenzimidazole in air; 2*b*) polybenzoylenebenzimidazole in helium.

Hitherto we have been seeing in most cases examples in which the presence of abnormal units impairs the properties of the polymer and is therefore undesirable. However, as we shall see below, there are also cases in which abnormal units improve the thermal, thermo-oxidative, and chemical stability of a polymer.

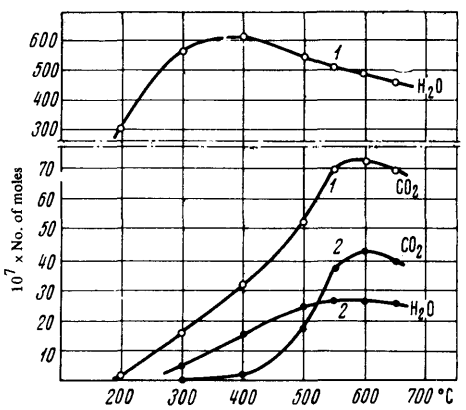


Figure 8. Evolution of water and carbon dioxide in the pyrolysis (15 mg in argon for 8 min) of:
1) poly(amide–amino acid); 2) pyrrone.

The presence of anomalous groupings has a very significant effect on the rate of the thermal depolymerisation of polyvinyl compounds, in most cases slowing it down significantly, as Dolgoplosk and other investigators have shown [179] on several polymers. This self-inhibition of the thermal decomposition of copolymers was shown by Dolgoplosk et al. [179,180] to be due to the difference in activity of the free radicals formed at the end of the chain. If if the radical ...–B· is more reactive, detachment of an A unit will require the consumption, not only of the energy evolved on addition of the monomer A, but also additional energy equal to the difference in energy between the two radicals, i.e. the energy of ...–B· minus the energy of ...–A·; breakdown is then retarded at the stage –A–B–A–A–A–.... If, however, the radical ...–B· is the less reactive, the slowing down occurs at the stage ·B–A–A–A–.... The depolymerisation rate curves in Fig. 9 support this deduction [180].

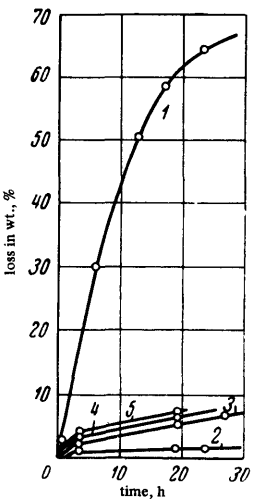
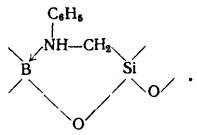


Figure 9. Kinetics of the degradation in air at 200 °C of copolymers of methyl methacrylate with:
1) poly(methyl methacrylate) alone; 2) citraconamide (40%); 3) methylmethacrylamide (40%); 4) hydroxymethylmethacrylamide (7%); 5) methacrylic acid (15%).

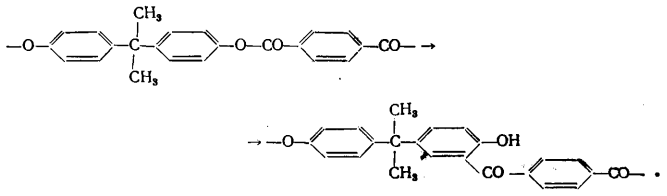
Because of this, copolymers of formaldehyde are also more thermostable than the homopolymer [181]. For the same reason polysilaphenylenesiloxanes are thermally more stable than polysiloxanes [182]. In these cases the

presence of foreign units has a favourable effect, by improving the thermal stability of the polymers.

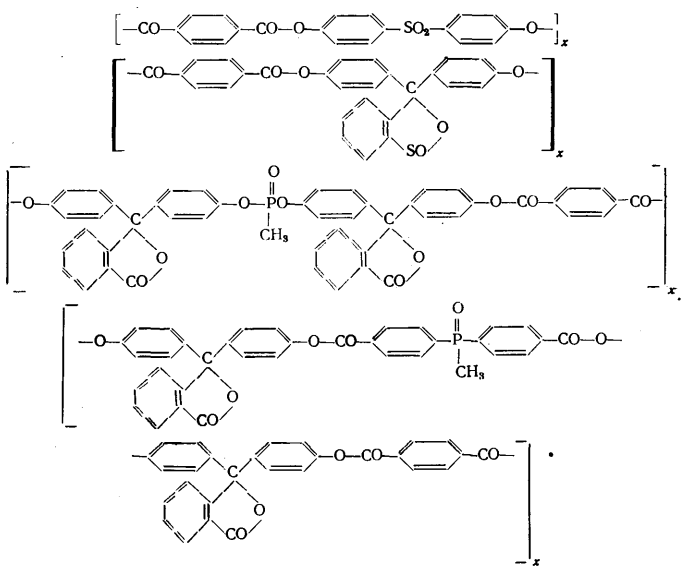
Andrianov's work [183], showing the substantial change in the properties of polymers produced by the introduction of small quantities of "alloying" additives, is most valuable for an understanding of the role of abnormal units. Thus he showed [184] that the presence of anilinomethyl groups attached to silicon greatly increases the hydrolytic stability of polyboraorganosiloxane copolymers, owing to formation of a donor–acceptor bond between boron and nitrogen



We find a similar situation in "self-protecting" polymers [147]. Under the influence of radiation or catalysts, self-protecting polyarenoates undergo the Fries rearrangement, with the formation [109,147] of hydroxybenzophenone units:



The presence of such groupings enhances appreciably the photochemical and the thermal stability of the polymers. A similar improvement in thermal stability is observed on the introduction into polyarenoates of units containing sulpho-groups and phosphine groupings, as in the compounds



Rafikov et al. [185,186] showed that the presence of such groups in these polyarenoates greatly increases their resistance to the action of light and heat.

IV. EFFECT OF ANOMALOUS MONOMER UNITS ON PHYSICAL PROPERTIES OF HETEROUNIT POLYMERS

The physical properties of polymers are also extremely sensitive to the presence of abnormal units, since the latter usually disturb the packing of the polymer chains, which interferes with their crystallisation and the formation of the most compact structures. This is very significant, since structure is a factor governing the physical and especially the mechanical properties of polymers [187]. The presence of abnormal units therefore diminishes the mechanical strength of fibres, films, and other articles made from a given polymer, and conversely raises the solubility and lowers the melting and softening points: i.e. their presence diminishes the heat resistance of polymers. In contrast to this, flawless polymers, containing no abnormal units, should obviously ensure denser packing of the chains, easy crystallisation of the polymer, very strong fibres, films, and other goods, high heat resistance, and sparing solubility.

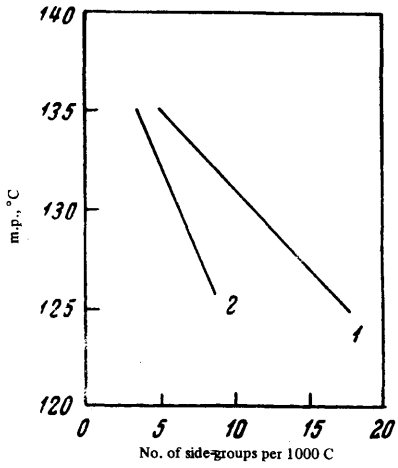


Figure 10. Melting-points of polymethylenes containing different quantities of alkyl groups: 1) methyl; 2) ethyl.

Some support for this suggestion may be found in Preston's work [188], which showed that fibres made from ordered copolymers have higher mechanical strength than fibres made from disordered copolymers with more imperfect heterounit macromolecules. This is suggested also by the effect of side-chains on the properties of polymers. Fig. 10 shows that increase in the content of methyl and ethyl groups lowers the melting point of copolymers [189], ethyl groups being the more effective.

The physical properties of three types of polyethylene (Table 3) show a fall in melting point and decreases in density and crystallinity with increasing degree of branching. The effect of abnormal units is exhibited especially clearly in polymers of butadiene and isoprene: *cis*-1,4-polymers possess the greatest elasticity; the presence of *trans*-1,4- and 1,2-units has an adverse influence on their properties.

Further support may be obtained from data on the effect of the relative imperfection of the structure of a polymer on its temperature characteristics, i.e. its heat resistance and thermal stability. Thus the glass and melting points of copolymers vary significantly with the quantity of the second monomer added [191-193]. Figs. 11 and 12 show a quite clear regularity for copolymers containing only small quantities of the second monomer. Fig. 11 shows the dependence of the glass point of vinyl polymers on the content of a second monomer [191]; Fig. 12 shows the composition dependence of the melting point of mixed polyamides [192,193]. In most cases both glass and melting points fall with increasing content of the second monomer, i.e. with increase in the number of abnormal units in the polymer chain. Since these temperatures depend on the strength of intermolecular forces, and hence on the degree of ordering of the macromolecules, their fall indicates that the second monomer diminishes the degree of order in the polymer and hence the forces of interaction between the macromolecules.

Table 3. Physical properties of various polyethylenes [190].

Property	Polymethylene	High-density polyethylene	Low-density polyethylene
Melting-point, °C	135	125	105—115
Density at 20°C, g cm^{-3}	0.97	0.95	0.92
Crystallinity, %	95	85	60—70

As we have seen, chemical defectiveness of the polymer structure may have a twofold effect on the physical properties: it may either weaken or strengthen intermolecular forces. This applies also to the rigidity of the macromolecules. In this case both the size and the polarity of a substituent are obviously significant. Fig. 13 shows how an abnormal unit containing a side-group or a branching affects the ordering of the macromolecules. The steric effect of a substituent will be in some measure proportional to its size. The final effect should depend also on the quantity of abnormal units. The influence of polarity will obviously be more clearly developed the more polar is the abnormal substituent in comparison with the main substituents, as is evident in a copolymer of vinyl chloride with acrylonitrile.

A clear example of the immense influence of the stereochemistry of units on the properties of a polymer is provided by the polyamides obtained from *cis*- and *trans*-cyclohexane-1,3-diamines with dicarboxylic acids. Fig. 14 shows the variation in melting point of the mixed polyamides containing various quantities of the *cis*- and *trans*-isomers [194]. The effect of the stereoisomerism is very clearly evident: polyamides obtained from the *trans*-diamine have higher melting points.

Chemical imperfection of the macromolecules is also an important factor governing the ability of polymers to crystallise. The more imperfect is a given heterounit polymer, i.e. the more abnormal units it contains and the more disordered their arrangement, the less is the tendency to crystallise under otherwise similar conditions.

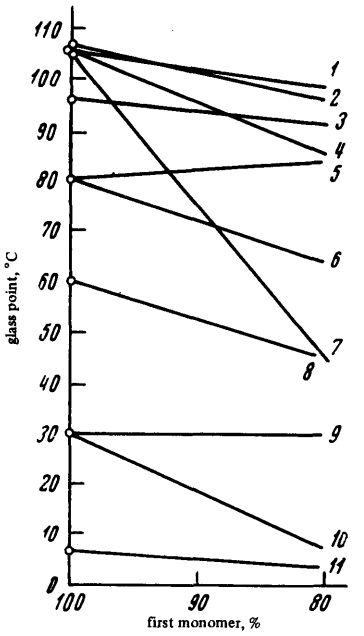


Figure 11. The effect of the nature and the quantity of the second monomer on the glass point of copolymers of:
1) methyl methacrylate with styrene;
2) acrylonitrile with methyl methacrylate;
3) styrene with methyl methacrylate;
4) methyl methacrylate with acrylonitrile;
5) vinyl chloride with acrylonitrile;
6) vinyl chloride with vinyl acetate;
7) methyl methacrylate with butyl acrylate;
8) ethyl methacrylate with butyl acrylate;
9) butyl acrylate with ethyl methacrylate;
10) butyl methacrylate with methyl acrylate;
11) methyl acrylate with butyl methacrylate.

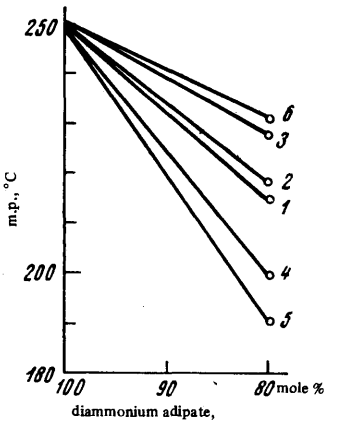


Figure 12. Dependence of melting point of mixed polyamides obtained from hexamethylenediammonium adipate on the nature and the quantity of the second component: 1) hexamethylenediammonium azela-ate;
2) hexamethylenediammonium sebacate;
3) hexamethylenediammonium pimelate;
4) *m*-phenylenediammonium adipate;
5) *m*-tolylenediammonium adipate;
6) 7-aminoheptanoic acid.

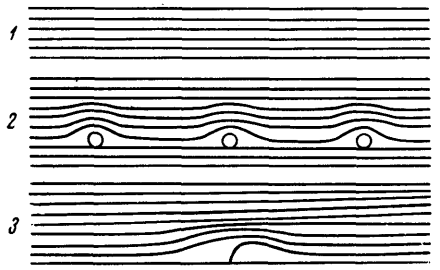


Figure 13. Diagrammatic illustration of effect of chemical defectiveness of macromolecules on their ordering: 1) perfect macromolecules; 2) macromolecules with side-chains; 3) macromolecules with branching.

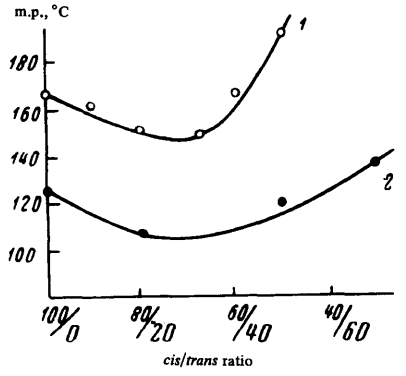
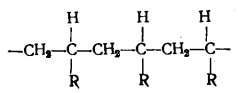
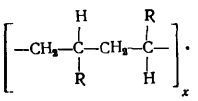


Figure 14. Variation of melting-point with ratio of *cis*- and *trans*-forms of cyclohexane-1,3-diamine for polyamides with: 1) adipic acid; 2) azelaic acid.

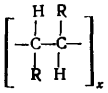
There are several polymers which it has not yet proved possible to obtain in a crystalline state. Among them must first be mentioned the atactic polymers of styrene, methyl methacrylate, propene, vinyl chloride, etc., which are amorphous owing to the disordered arrangement of *dextro*- and *laevo*-units in their macromolecules. In this sense they are also copolymers of the stereoisomeric *dextro*- and *laevo*-forms of the units. When arranged with some regular alternation, however, these same monomer units give readily crystallisable homopolymers—the isotactic polymers



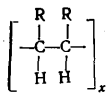
and also a regular copolymer of *dextro*- and *laevo*-forms—a syndiotactic polymer—which, however, can be regarded also as a homopolymer having the longer unit



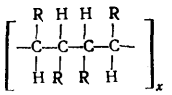
Similarly, the di-isotactic *threo*-polymer



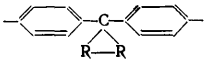
and the di-isotactic *erythro*-polymer



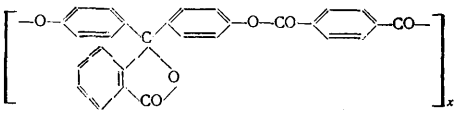
are homopolymers, whereas the disyndiotactic polymer can be regarded either as a copolymer of two different units or as a homopolymer having the longer unit



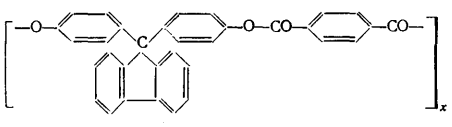
Several polycondensation polymers exhibit a similar effect of monomer structure on ability to crystallise. Thus polyarenoates that are polyesters of dihydric phenols and dicarboxylic acids containing rings and a central carbon atom, of the type



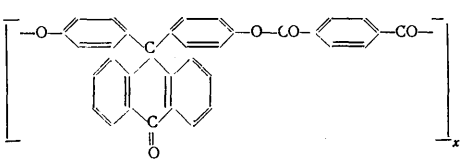
are among the most interesting "card" polymers. They are constructed on the necklace principle: i.e. each unit contains a carbon atom forming part both of the polymer chain and of a side-ring. These polyarenoates are either crystalline or amorphous depending on their structure. Polyarenoates of phenolphthalein having the structure



are non-crystallisable, amorphous polymers [144]. This was explained on the hypothesis that their structure resembles that of atactic polymers: i.e. they have a statistical distribution of an asymmetric substituent (phthalide group) in the repeating unit of such a polyarenoate, which is a heterounit polymer (Section II, 4). Under certain conditions a stereoregular distribution of this substituent could probably be achieved, which would lead to the formation of a crystalline polyarenoate of phenolphthalein. This suggestion is supported by our observation [144] that polyarenoates of card type having a symmetrical cyclic side-substituent are able to crystallise. Examples are the polyarenoates based on 9,9-bis-*p*-hydroxyphenylfluorene (I) and 10,10-bis-*p*-hydroxyphenylanthrone (II)



(I)



(II)

These polyarenoates are crystalline substances, in contrast to those of phenolphthalein.

Similarly, as Batzer showed [195], poly(hexamethylene 2,9-dibutyldecanedioate) does not crystallise, in contrast to the crystalline poly(hexamethylene decanedioate). The reason is that the former polyester is also an atactic heterounit polymer, because the racemic form of the initial acid was taken, so that the polymer has an irregular distribution of butyl groups. The copolymer obtained from decanedioic and 2,9-dibutyldecanedioic acids begins to crystallise only when their proportions are 5 : 1, which corresponds to a content of one butyl group for every 54 atoms in the polymer chain [195]. In this case the presence of abnormal units becomes sufficiently minor not to prevent crystallisation of the polyester.

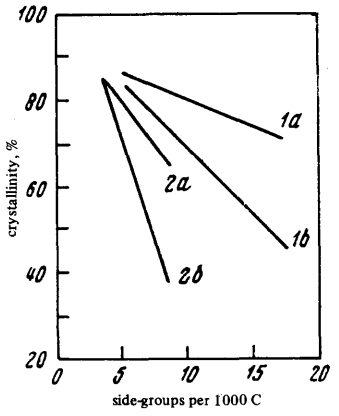


Figure 15. Crystallinity of branched polymethylenes determined by different methods:
1*a*) methyl groups by X-ray examination;
1*b*) methyl groups by differential thermal analysis;
2*a*) ethyl groups by X-ray examination;
2*b*) ethyl groups by differential thermal analysis.

We may recall also that, when carbyne is heated to 1000°C, the abnormal units

$$-C\equiv C-CH=C=C=,$$

split off hydrogen

$$-C\equiv C-CH=C=C= \xrightarrow{-H} -C\equiv C-C\equiv C-C\equiv C-$$

which results in conversion of the polymer into a crystalline form [114]. As a consequence of this reaction, the heat-treatment of carbyne enhances its crystallinity.

A detailed investigation of the dependence of crystallinity on the number of abnormal groups has been made on polymethylenes containing various quantities of methyl or ethyl groups, obtained by copolymerising diazomethane with diazoethane or diazopropane [189]. Fig. 15 shows that ethyl groups have a stronger effect than methyl groups in diminishing crystallinity. The amorphous content is greatly increased by the presence of branching in the polyethylene macromolecules (Fig. 16) [196].

The density of polymers changes significantly with increasing imperfection of the macromolecules: it usually decreases with increase in the content of abnormal units. The presence of branches has a similar effect: thus unbranched polymethylene has a density of 0.971, slightly branched low-pressure polyethylene 0.95–0.96, and strongly branched high-pressure polyethylene 0.92 to 0.93 (Table 4). The densities of copolymers obtained from diazomethane and other diazoalkanes [189] are also given in Table 4, from which it is evident that increase in the number and length of the side-chains diminishes the density of the polymer. The variation in the density of polyethylene with degree of branching illustrated in Fig. 17 shows a decrease in density with increase in content of methyl groups [197].

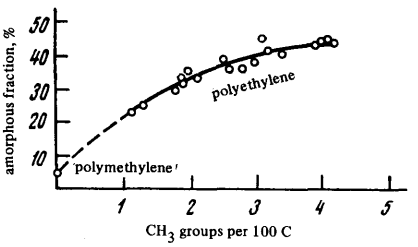


Figure 16. Dependence of content of amorphous material on degree of branching of polyethylene macromolecules.

The solubility of polymers also is extremely sensitive to the presence of abnormal units in the macromolecule: it is usually increased by increase in their content and their disordered arrangement. This is illustrated (Fig. 18) by the dependence of the temperature of dissolution of polymethylenes containing branched macromolecules on the number of branches [16].

Table 4. Properties of copolymers.

Polymeric material	Mode of preparation	Density
Polymethylene	polymerisation of diazomethane	0.971
Polymethylene with side-groups:		
methyl	diazomethane–diazoethane copolymer	0.939
ethyl	diazomethane–diazopropane copolymer	0.952
Polyethylene with ethyl side-chains	ethylene–but-1-ene copolymer	0.957
Crystalline ethylene–propene block copolymer	copolymerisation of ethylene and propene	0.917

Enhancement of solubility is observed also in many copolymers. Homopolyamides usually dissolve only in acids, phenols, and amides, whereas their copolymers and mixed polyamides dissolved even in aqueous alcohol. Fig. 19 shows how the solubility of mixed polyamides varies with their composition [198].

We have thus been considering many of the methods for synthesising polymers known at the present time, and have shown that they are all accompanied by various side-reactions. These result in the formation of abnormal units in the macromolecule, and the consequent chemical defectiveness characteristic of heterounit polymers. Abnormal units appear not only during polymerisation and polycondensation but also in the course of copolymerisation and copolycondensation.

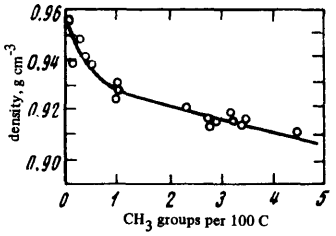


Figure 17. Dependence of density of polyethylene on degree of branching.

Various reactions involving substitution in the polymer chain also lead to the appearance of abnormal units and the formation of heterounit polymers. It is undoubtedly possible to influence the number and distribution of the abnormal units thus formed, which is an important task of synthetic polymer chemistry. The significance of studying the chemical imperfection of the macromolecule structure is that it has a great influence on the chemical and physical properties of polymers, as has been illustrated by the series of examples of heterounit polymers given here.

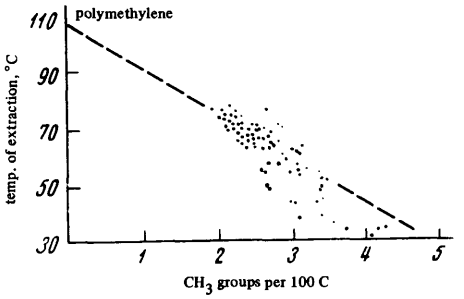


Figure 18. Dependence of temperature of dissolution on degree of branching of polyethylene macromolecules.

Finally we conclude that these examples quite clearly illustrate the effect of various reactions leading to the formation of abnormal units and hence the production of heterounit polymers of general formula $[[M]_m-[A]_n]_x$.

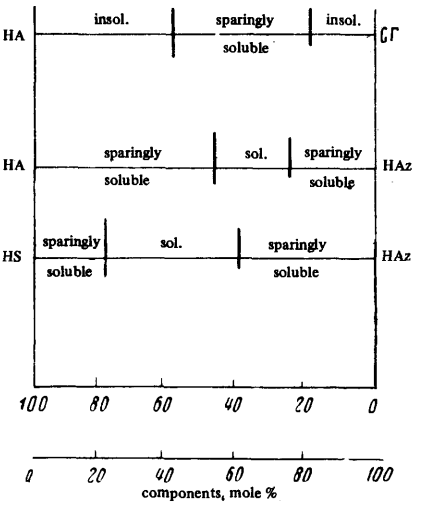


Figure 19. Effect of composition of copolymers on their solubility in ethanol: HA = hexamethylenediammonium adipate; HS = hexamethylenediammonium sebacate; HAz = hexamethylenediammonium azela-ate.

This feature of polymerisation and polycondensation processes, and also of substitution in polymer chains, has not yet been investigated systematically, so that our knowledge in this field is still largely haphazard. However, it can be concluded from the above results that almost all real polymers comprise heterounit macromolecules, while homounit polymers, containing no abnormal units, are rare exceptions. Hence this must be taken into account in considering the problem of the relation between the structure and the properties of polymers, since the concept of heterounit polymers as the main type of polymeric structure acquires fundamental importance for polymer chemistry.

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Institute of Organoelementary Compounds, USSR Academy of Sciences, Moscow

U.D.C. 547.933:

Degradation of Cellulose by Alkaline Oxidation

O.P.Golova and N.I.Nosova

Investigations on the alkaline and oxidative-alkaline degradation of cellulose by molecular oxygen are reviewed, and the reaction mechanisms are surveyed. The effect of the supermolecular structure of cellulose on the rates of these processes is examined. A list of 136 references is included.

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I. INTRODUCTION

The problem of the oxidative degradation of cellulose embraces a very wide range of scientific and practical questions—oxidising reactions, the effect of chemical and supermolecular structure on the oxidation of cellulose, the changes in chemical, physical, and mechanical properties of cellulose produced by oxidants, etc. The present Review discusses aspects of the alkaline and oxidative–alkaline degradation of cellulose and the mechanisms of the reactions involved.

II. ALKALINE DEGRADATION OF CELLULOSE AND OXIDISED CELLULOSES

The oxidation of cellulose by molecular oxygen in alkaline media is a very complicated process, involving genuine oxidation reactions and also reactions undergone by the initial cellulose and its oxidation products under the influence of alkalis. In order to obtain a better understanding of this complicated question, it is advisable firstly to consider the reactions occurring during the alkaline degradation of cellulose and oxidised cellulose.

The reactions involved in the degradation of carbohydrates under the influence of alkalis are also very complicated, and have been discussed in detail in several review papers and monographs [1-8]. We therefore give only the principal experimental results together with modern views on the mechanism of the reactions involved.

1. Alkaline Degradation of Cellulose

The main processes occurring in the alkaline degradation of cellulose are the so called degradation of cellulose from the reducing end of its molecule and the alkaline hydrolysis of glycosidic bonds. The former process is observed almost exclusively at temperatures up to 150°C; the two processes occur simultaneously above this temperature.

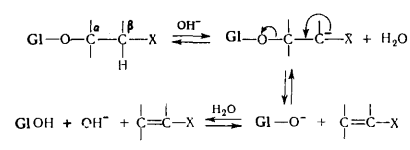
(*a*) Degradation of cellulose from the reducing end

The action of alkalis on cellulose at temperatures up to 150°C produces losses in weight without any considerable change in the degree of polymerisation [9,10]. Native cotton cellulose reacts slowly with a hot alkali solution, but the rate increases when the degree of polymerisation is lowered by hydrolysis, with a resulting increase in the number of aldehyde groups. On the basis of these observations Davidson suggested [11] that degradation consists in the successive detachment of units from the end of a molecular chain possessing reducing properties. The validity of this hypothesis has since been confirmed by numerous experimental data. It has been shown that hydrocelluloses are degraded more rapidly than cotton cellulose, though having the same chemical structure but a lower degree of polymerisation; the rate of degradation of hydrocelluloses increases as the degree of polymerisation falls, and hence as the content of reducing terminal groups decreases [10,12]. The stability of hydrocellulose towards hot dilute alkali is sharply improved when the aldehyde end-groups are eliminated by being oxidised to carboxy-groups with chlorous acid [13], bisulphite solutions at high temperatures [14], or cuprammonium solutions [15], reduced with sodium tetrahydroborate in weakly alkaline medium [10,16], dehydrated by heating [17], or even modified by glycoside formation [18].

Breakdown from the reducing end is indicated also by data suggesting that acids of approximately the same composition are formed by the action of alkalis on hydrocellulose and on 4-*O*-substituted monosaccharides and 1,4-disaccharides [19].

(*b*) Mechanism of degradation from the reducing end

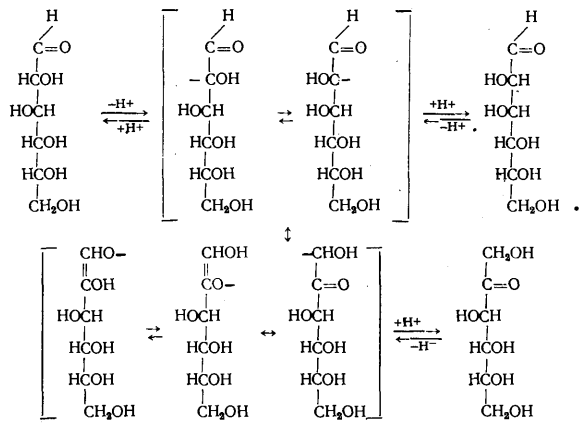
The most widely accepted explanation of the alkaline degradation of cellulose from the reducing end is based on Isbell's theory of β-elimination [20], which he proposed to explain the previously observed [21,22] instability towards alkalis of glycosides of alcohols containing electronegative groups in the β-position. The reaction is represented by



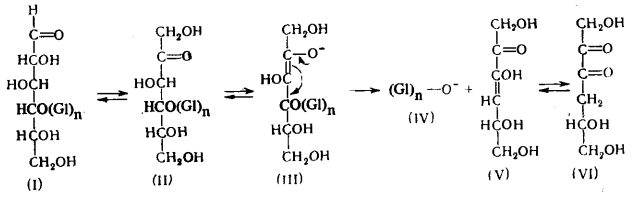
This theory is widely used at the present time to explain the sensitivity to alkalis of unsubstituted and substituted monosaccharides and also of di-, oligo-, and polysaccharides [19,23-35].

According to Isbell's theory an alkoxy-group should be present in the β-position relative to the aldehyde group. In the reducing terminal unit of cellulose the alkoxyl is in the γ-position to the aldehyde group. Detachment of the reducing terminal glucose unit will become possible after isomerisation into a fructose unit [9,23]. The possibility of the conversion of monosaccharides into their epimers and the corresponding ketoses by the action of alkalis had already been shown at the end of the nineteenth century by Lobry de Bruyn and van Ekenstein [36]. Not only monosaccharides but also the reducing units of disaccharides, oligosaccharides [37-40], and cellulose [23] are able to undergo similar transformations.

The most probable mechanism of this rearrangement [36] involves elimination of a proton and formation of a carbanion in equilibrium with enolate ions; the latter have a planar configuration and are converted with almost equal probability into three epimers [41]:

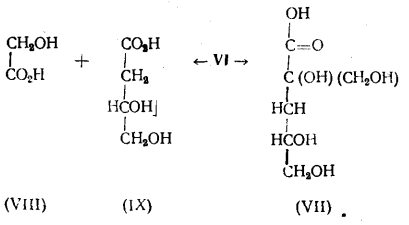


The degradation of cellulose by the action of alkalis is regarded [23] as involving conversion of a reducing terminal unit (I) of cellulose into a fructose unit (II), which is detached as the enolic form (V) of a dicarbonyl compound:



This liberates a reducing group in the adjacent glucose unit, which in turn undergoes the same changes. Thus a stepwise process of alkaline degradation takes place, beginning from that terminal unit of the cellulose molecule that possesses reducing properties.

The eliminated enol (V) undergoes further changes, the composition of the products depending on the nature of the alkali and the reaction conditions. Calcium hydroxide yields mainly D-glucoisosaccharinic acid (VII), whose formation results from rearrangement of 4-deoxy-D-*glycero*-2,3-hexodiulose (VI), which has been isolated from and identified in the products of the alkaline degradation of cellobiose [31] and maltose [32]:



Treatment with caustic soda favours conversion of (VI) into a mixture of $\beta\gamma$-dihydroxybutyric (IX), glycollic (VIII), formic, and lactic acids [19,32].

(*c*) "Stopping" reactions

The alkaline degradation of cellulose never goes to completion, and the final polysaccharide becomes stable towards alkali [10]. This stability is due to conversion of the usual reducing terminal glucose units into non-reducing units containing carboxy-groups [42,43]. Richtzenhain and Abrahamsson [44] considered that the reducing terminal units might rearrange into saccharinic acids, whereas Lindberg [45] assumed that the carboxyls were formed either by oxidation of the reducing groups by traces of oxygen or as a consequence of a Cannizzaro reaction between aldehyde groups of the terminal unit and those of soluble decomposition products.

The nature of the stabilising reaction was investigated by Machell and Richards [9,35], who subjected alkali-stabilised hydrocellulose to acid hydrolysis and isolated the acidic products. The main product was identified as D-metasaccharinic acid, whose formation during alkaline treatment might be a consequence of β-elimination of the 3-hydroxyl in the terminal glucose unit followed by rearrangement of the resulting enol. Because of the absence of a carbonyl group, hydrocellulose molecules containing metasaccharinic acid as terminal unit are stable towards alkali.

Alkaline-earth metal ions—Ca^{2+}, Sr^{2+}, Ba^{2+}—are evidently more effective than sodium ions in catalysing the conversion of reducing terminal units in cellulose into metasaccharinic acid redidues [12,33,46]. Stabilisation is usually slower than degradation from the reducing end. The activation energies for the degradation of hydrocellulose from the reducing end by the action of 5% sodium hydroxide solution (in the absence of oxygen) and for the formation of stable terminal metasaccharinic acid units are 24 and 32 kcal mole^{-1} respectively [47].

It is interesting that the 3-deoxy-D-*erythro*-hexulose postulated by Isbell's theory as an intermediate in the formation of metasaccharinic acids has been isolated and identified by Machell and Richards [34] on treating 3-*O*-benzyl-D-glucose with 0.04 *N* sodium hydroxide. On treating with calcium hydroxide solution the isolated reaction intermediate was converted almost quantitatively into D-glucometasaccharinic acid [34].

(*d*) Alkaline hydrolysis of glycosidic bonds

Solutions of alkalis at 170°C and above cause the direct hydrolysis of cellulose, which is indicated by a rapid drop in degree of polymerisation and considerable weight losses [48,49]. This reaction is due to the action of hydroxide

ions, not to oxidation by traces of oxygen or to a purely thermal effect [49]. Brooks and Thompson [50] used methyl β-glucoside to show that 10% sodium hydroxide solution produces a very low rate of rupture of glycosidic bonds (after 5 h only 0.3%, 0.9%, and 5.5% of glycosidic bonds broken at 140°, 150°, and 170°C respectively).

Investigation of the alkaline hydrolysis of glycosides by Lindberg and his coworkers [45, 51-54] on numerous model compounds showed the simultaneous occurrence of several reactions. Thus the action of 10% sodium hydroxide solution on 4-*O*-β-D-glucopyranosyl-D-sorbitol yields 1,6-anhydro-β-D-glucopyranose, D-sorbitol, 1,4-anhydro-D-sorbitol, and acidic products. Formation of the first two products necessitates rupture of the bond between the glycosidic oxygen and the $C_{(1)}$ atom of the glucose residue; formation of the third product requires rupture of the corresponding bond with the $C_{(4)}$ atom of the sorbitol residue. Direct attack by a hydroxide ion on these carbon atoms may give glucose and sorbitol respectively. Under the experimental conditions glucose rapidly forms acidic products.

The alkaline hydrolysis of cellulose forms new reactive groups for ensuring degradation from the reducing end, which occurs by the same mechanism as at lower temperatures. The soluble breakdown products obtained when cotton cellulose is treated with 0.5 *N* sodium hydroxide solution at 170°C include the same compounds as produced by treating hydrocellulose with a 0.5 *N* solution of the alkali at 100°C. [49]

2. Alkaline Degradation of Oxidised Celluloses

Since oxidation and alkaline degradation occur simultaneously, it is useful first to examine the alkaline degradation of already oxidised cellulose. Alkalis break down the structure of oxidised celluloses. Davidson investigated the oxidation of cellulose with potassium dichromate in an acid medium, and found that the viscosity of a solution of oxidised cellulose nitrate is far higher than that of oxidised cellulose in cuprammonium solution. This difference disappears after treatment of the oxidised cellulose with alkali [55]. Furthermore, oxidised celluloses lose weight when heated with weak solutions of alkalis [56]. Staudinger and Sohn [57] attributed the lowering of the degree of polymerisation of cellulose to the presence of ester bonds in its chain, which are cleaved by the action of alkalis. They also discussed the ways in which ester bonds are formed on oxidation.

Somewhat later, investigators came to link the degradation of oxidised celluloses by the action of alkalis with the formation of carbonyl groups, which facilitate the rupture of glycosidic bonds [58, 59]. Oxycelluloses obtained by periodate oxidation, and hence containing aldehyde groups at positions 2 and 3 of the repeating unit of cellulose [60], are easily degraded by alkalis [13, 56, 61-63], the sensitivity to which increases with increase in the content of aldehyde groups [61, 63]. According to Kaverzneva and Ivanov the fall in the viscosity of cellulose when oxidised with air in cuprammonium solution is due to rupture of glycosidic bonds caused by the presence of aldehyde groups formed by the oxidation of primary alcoholic groups [64].

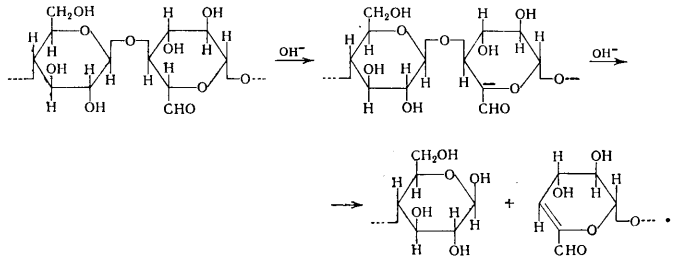
The influence of ketonic groups on the stability of cellulose oxidised with dichromate was referred to by Meller [13]. Kaverzneva and Kist' [65] showed that the presence of a considerable quantity of ketonic groups in cellulose oxidised with nitrogen dioxide is the main reason for its degradation in alkaline media.

The dominant effect of carbonyl groups on the degradation of oxidised cellulose in an alkaline medium is evident also from the conversion of alkali-unstable oxidised celluloses into stable materials by reduction with sodium tetrahydroborate in a weakly alkaline medium, i.e. under conditions such that aldehyde groups are converted into alcoholic groups [61-63, 66]. The stability of oxidised celluloses is considerably enhanced also when carbonyl groups are oxidised to carboxy-groups [13, 62].

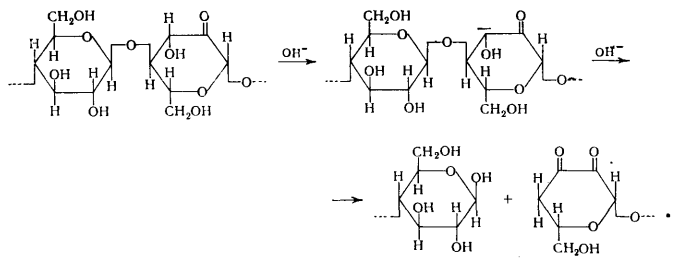
(*a*) Mechanisms of the degradation of oxidised celluloses

Several reaction mechanisms have been suggested [58, 64, 67, 68] to explain the alkaline degradation of oxidised celluloses, but investigations during recent years of the degradation of these materials, as well as of monosaccharides, disaccharides, and their derivatives, have shown that, when a carbonyl group is present in the β-position relative to a glycosidic bond, degradation takes place mainly by Isbell's mechanism [69].

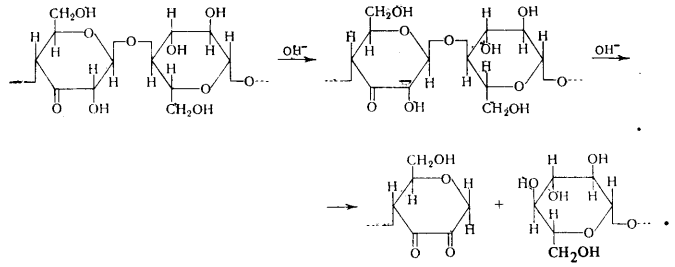
This hypothesis was first put forward by Haskins and Hogsed [59], who gave the following scheme for the alkaline degradation of cellulose containing units with a 6-aldehyde group



When the alcoholic group at $C_{(2)}$ of the repeating unit of cellulose is oxidised, the mechanism of cleavage of the glycosidic bond under the influence of alkali will be

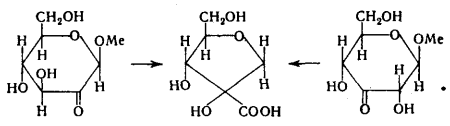


The action of alkali on cellulose containing units with a 3-keto-group should be represented by



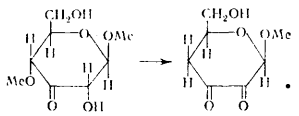
A later investigation of the action of alkali on model compounds having a keto-group at the $C_{(2)}$ and $C_{(3)}$ atoms—methyl β-D-*arabino*-hexulopyranoside (X) and methyl

β-D-*ribo*-3-hexulopyranoside (XI)—showed [70] that they rapidly split off the methoxy-group under the influence of weak solutions of sodium or calcium hydroxide at room temperature. The same final product (XII) is obtained in the two cases, whence it follows that the intermediate product is the same in the two reactions:



(X) (XII) (XI)

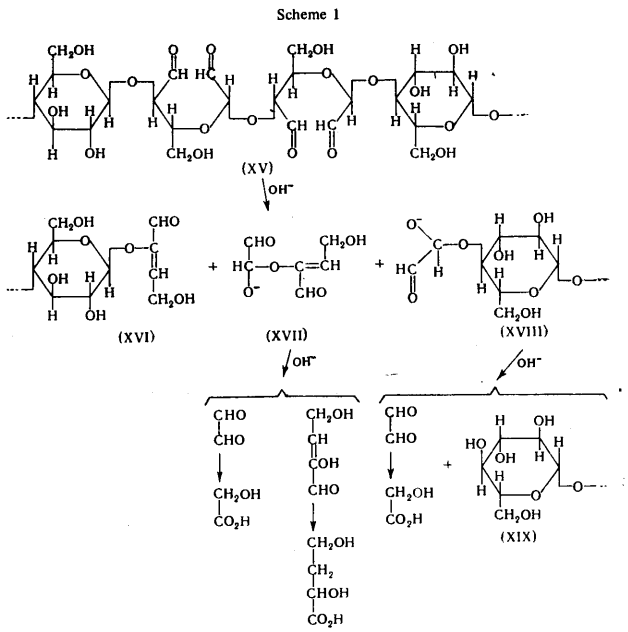
In order to determine whether, in the alkaline treatment of cellulose containing glucose units with a keto-group at $C_{(2)}$or $C_{(3)}$, elimination occurs at the glucosidic carbon atom or at the $C_{(4)}$ atom, the alkaline degradation of methyl 4-*O*-methyl-β-D-*ribo*-3-hexulopyranoside (XIII) was examined [71]. This compound is degraded almost five times as rapidly as (XI). The chief intermediate product is isolated in the degradation of (XIII) was the 4-deoxy-compound (XIV):



(XIII) (XIV)

From this the author concluded that the alkaline degradation of oxidised cellulose of this type involves the cleavage mainly of bonds between the $C_{(4)}$ atoms of the glucose units and the oxygen of the glycosidic bonds.

Scheme 1



Model compounds—methyl 4-*O*-methyl-β-D-*arabino*-hexulopyranoside, methyl 4-*O*-methyl-β-D-*ribo*-3-hexulopyranoside, and methyl 6-formyl-4-*O*-methyl-β-D-glucopyranoside—were used to study the effect of different positions of the carbonyl group in the oxidised glucose unit. The glycosidic bond was found to be most labile in compounds containing a carbonyl group in position 2 or 3. It was more stable in compounds containing a 6-aldehyde group [71].

O'Meara and Richards [69] examined the initial and final products of the alkaline degradation of periodate-oxidised cellulose, and concluded that degradation occurs mainly by Isbell's β-alkoxy-carbonyl mechanism. When periodate oxycellulose is treated with calcium hydroxide solution the chief products are glycollic and αβ-dihydroxybutyric acids, the relative proportion of the former acid diminishing with increasing degree of oxidation of the cellulose. These workers give Scheme 1 for the degradation of periodate-oxidised cellulose.

Three cleavage products (XVI)–(XVIII) are formed initially. The first of these is fairly resistant to the further action of alkali. Products (XVII) and (XVIII) are glyoxal hemiacetals, and are rapidly cleaved by lime-water at room temperature: (XVII) gives equivalent quantities of glycollic and αγ-dihydroxybutyric acids; and (XVIII) yields glycollic acid and a normal, non-reducing terminal glucose unit (XIX). The possibility of such breakdown is supported by a study of the properties of glyoxal hemiacetals [69] and of the alkaline decomposition of model compounds [72]. The ratio of the quantities of glycollic and αγ-dihydroxybutyric acids for cellulose preparations of different degrees of oxidation also supports reaction in this direction, since only the product (XVII), which is formed at a high degree of oxidation of the cellulose, is a source of αγ-dihydroxybutyric acid.

III. OXIDATION OF CELLULOSE BY MOLECULAR OXYGEN IN ALKALINE MEDIA

In the preceding Sections of the Review we have isolated and examined aspects of the alkaline degradation of cellulose and oxycelluloses. We now give an account of published information on the simultaneous oxidative and alkaline degradation of cellulose. The oxidation of cellulose by air in alkaline media can take place both under heterogeneous and under homogeneous conditions. Processes involving the heterogeneous oxidation of cellulose are especially widespread, taking place both in the isolation and processing of cellulose and during the functioning of goods made from it. The Review will be confined to aspects of the heterogeneous oxidation of cellulose.

Most of the many publications on the oxidation of cellulose by molecular oxygen in an alkaline medium are concerned with the investigation of oxidation under the conditions of ripening in the manufacture of viscose rayon. We shall first give the experimental results obtained by various investigators on the oxidation of cellulose by molecular oxygen in alkaline media, and then consider views on the chemical changes undergone by the cellulose macromolecule and the suggested reaction schemes.

1. Process Characteristics of the Oxidation of Cellulose

The autoxidation of cellulose in alkaline media has been followed experimentally by examining the rate of absorption of oxygen, the variation in degree of polymerisation and in functional groups, and the chemical composition of the resulting cellulose and decomposition products of low molecular weight. The first fact to emerge from an examination of these results is that the rate and several features of the oxidation depend in considerable measure on whether the cellulose has been squeezed free from

excess of alkali or whether oxygen is passed through caustic soda solution containing cellulose in suspension. For the sake of brevity we shall henceforward term the former process the "oxidation of alkaline cellulose", and the latter the "oxidation of a cellulose suspension". When discussing the autoxidation of alkaline cellulose the alkali concentration will not be indicated if 18–20% solutions of caustic soda were used for impregnation. The oxidation of a suspension of cellulose is slower than that of alkaline cellulose.

Mention should be made of the difficulties of comparing results obtained by different workers, resulting from the use of different samples of cellulose, obtained not only from different types of raw material but also by different methods of isolation and purification, and resulting also from the use of different methods for determining functional groups and different degrees of polymerisation of the cellulose. Different methods often give different results.

Here we shall not consider the defects of methods for determining functional groups in cellulose, but merely cite the literature on this problem. Critical surveys of such methods will be found in monographs[3,73,74]. Analytical results for carbonyl groups obtained by various methods have been compared by the Sihtola[75], Strole[76], and Gunne and Samuelson[77]. Different methods for determining the copper numbers of cellulose were compared by Bethge and Nevell[78], and copper numbers have been compared with the content of carbonyl groups determined by the hydroborate method[79]. Various methods have been given[80,81] for determining carboxy-groups.

(*a*) Absorption of oxygen

The chief parameter indicating the rate of autoxidation of cellulose is the rate of absorption of oxygen. It must be borne in mind, however, that the oxygen absorbed is consumed not only in the primary oxidation of cellulose macromolecules but also in the oxidation of secondary products of low and high molecular weight, formed as a result of oxidative–alkaline degradation. The rate curves for the absorption of oxygen during the oxidation of alkaline cellulose comprise three portions: the rate varies during the first period, after which it remains constant, and during the third period it falls[82–84].

For any given type of cellulose the initial rate of absorption of oxygen during oxidation of the alkaline material is proportional to the copper number of the regenerated cellulose. The same dependence is shown by cotton cellulose bleached with hypochlorite, hydrocellulose obtained from cotton cellulose, and various wood celluloses. The initial rate of absorption of oxygen by periodate-oxidised cellulose is about half the rate for cotton cellulose and other celluloses having the same copper numbers as the periodate-oxidised sample. A diminished initial rate of absorption of oxygen was observed also for cellulose that had first been subjected to oxidation by molecular oxygen in an alkaline medium. If oxidation was interrupted during the constant-rate period, and the regenerated cellulose was again subjected to oxidation, the rate of absorption of oxygen was very low, far below the steady rate, although the regenerated cellulose had a high copper number. The explanation offered was that probably not all, only a proportion, of the reducing groups of cellulose are capable of initiating its oxidation[84].

In some cases oxidation progresses autocatalytically during the first period: i.e. the rate of absorption of oxygen increases with the duration of oxidation. Purified cotton cellulose, of low reducing power, is oxidised autocatalytically. In other cases the rate of absorption of oxygen gradually decreases, as in the oxidation of wood celluloses of higher reducing power[84]. Sometimes the rate of absorption of oxygen remains constant from the start of oxidation, as with alkaline purified beechwood cellulose[82].

During the second period of oxidation the rate of absorption of oxygen is constant and about the same for different alkaline celluloses, in spite of differences in reducing power[84]. The rate remains constant until the total absorption is ~0.6 oxygen atom per anhydroglucose unit of the cellulose[84].

With increase in the alkali concentration the rate of absorption of oxygen by alkaline cellulose increases, passes through a maximum, and decreases with further increase in concentration. Weltzien and Tobel[85] observed the maximum rates at alkali concentrations of 6.5 *N* and 8.5 *N* for cotton cellulose and for cellulose hydrate regenerated from cuprammonium solution respectively, and Davidson[83] found the optimum for cotton cellulose to be 10 *N* caustic soda. With wood cellulose the maximum rate of absorption of oxygen is found at a concentration of the impregnating alkali of 10–12.5 *N*.[84]

Not only the rate of absorption of oxygen but also the character of the rate curves changes with the alkali concentration for the same cellulose preparation. At alkali concentrations below 8 *N* the initial rate exceeds the steady value in the oxidation both of alkaline cellulose and of a suspension of cellulose; above 8 *N*, however, the initial rate is lower than the steady rate[84,86]. In the oxidation of a suspension of cellulose, in contrast to that of alkaline cellulose, the rate of absorption of oxygen increases continuously with increase in the alkali concentration[86].

A rise in temperature produces an increase in the rate of absorption of oxygen[83–85]. According to Davidson[83] the rate increases approximately ninefold when the temperature of the oxidation of alkaline cotton cellulose is raised from 20° to 40°C. Entwistle et al.[84] calculated the activation energy as ~21 kcal mole^{-1} for sulphite wood cellulose during the period of a steady rate of absorption of oxygen by the alkaline material at temperatures from 5° to 80°C. This value corresponds roughly to a threefold increase in reaction velocity for a 10-deg rise in temperature.

Increase in the oxygen pressure from 25 to 700 mmHg produces an increase in the rate of absorption. At higher alkali concentrations the rate is more strongly dependent on pressure[84,86].

Salts of various metals present in low concentrations in cellulose have an appreciable catalytic effect on its rate of oxidation. Those of iron[87], copper[83], nickel[83], cobalt[86], and manganese at a manganese concentration of 0.002% (on the cellulose)[87,88] are positive catalysts. The greatest effect is exerted by salts of cobalt, followed by manganese, iron, nickel[88], and copper[89]. Gold and silver salts are inhibitors, as also manganese salts at manganese concentrations exceeding 0.05%.[88] Neither catalytic nor inhibiting metal salts have any appreciable effect on the initial rate of absorption of oxygen, but affect it during subsequent stages of the reaction[88].

The addition of substances that form free radicals increases the initial rate of absorption of oxygen[88].

Addition of 0.1% of a typical antioxidation to the impregnating alkali lowers appreciably the steady rate of absorption of oxygen. 1,4-Naphthaquinone and magnesium diphenylamine-*p*-sulphonate were most effective[88].

These antioxidants did not influence the initial rate of absorption.

The initial rate is increased by adding to the impregnating alkali substances capable of autoxidation, such as glucose, formaldehyde, sodium dithionite, etc.[88]

If oxidation is interrupted by removing oxygen from the reaction space, and is then renewed, the original rate of absorption of oxygen is re-established[82,83].

(*b*) Variation of degree of polymerisation of cellulose during oxidation in alkaline media

The degree of polymerisation of cellulose usually drops sharply at the beginning of oxidation, but the rate of depolymerisation then diminishes[84,90-93]. A high rate of depolymerisation during the initial period is observed[94-96] in celluloses having a comparatively high content of carbonyl groups and hence high copper numbers (0.58 to 1.04 according to Brady). In celluloses having low contents of carbonyl groups (Brady copper numbers 0.10–0.18) the rate of depolymerisation remained constant for 24 h. Reduction with sodium tetrahydroborate to diminish the content of carbonyl groups in wood celluloses only slightly decreases the rate of depolymerisation during the first period of oxidation. During the following period the rates for reduced and unreduced cellulose converge, with the rate for celluloses in which the carbonyl groups have been reduced remaining constant[94].

Good agreement was shown[84] between the initial rate of absorption of oxygen by alkaline wood celluloses and the rate of decrease in viscosity, as well as the same ratio of change in viscosity to quantity of oxygen absorbed by alkaline cotton cellulose of varying reducing power. Schulz and Mertes[82] compared their kinetic data on oxygen absorption with the variation in degree of polymerisation during the oxidation of alkaline cellulose at 20°C. They observed a rapid fall in degree of polymerisation at the start of the oxidation of alkaline cotton cellulose, after which depolymerisation slowed down, and a constant rate was established after about 15 h. The rate of absorption of oxygen became constant 100 h after the start of oxidation. In the oxidation of beechwood cellulose under the same conditions the rate of depolymerisation was constant from the very beginning.

The rate of depolymerisation of cellulose during oxidation depends on the caustic soda concentration. At low alkali concentrations cellulose is depolymerised very slowly. For example, the degree of polymerisation hardly changes during the oxidation of a cellulose suspension in 1% and 2% caustic soda solution at 40°C,[97] and varies very slightly during oxidation at 85–86°C.[98] With alkali concentrations up to 80 g litre^{-1} no change in degree of polymerisation occurs for 2 h during the oxidation both of alkaline cellulose and of a cellulose suspension at 50°C. With increase in the caustic soda concentration the rate of depolymerisation of cellulose passes through a maximum according to some investigators[86,99,100] but exhibits a continuous increase according to others[83,89]. The reasons for the discrepancies are obscure.

The rate of depolymerisation of cellulose increases with rise in temperature[99,101,102]. It has been suggested that the mechanism of degradation in the oxidation of alkaline cellulose is probably the same at different temperatures (25° and 50°C), a difference being observed only in the rate of degradation[103].

Catalysis of the oxidation of alkaline cellulose by transition-metal compounds or free radicals is accompanied by increase in the degree of depolymerisation for a given absorption of oxygen[83,88]. In the presence of silver and organic antioxidants the degree of depolymerisation at a given oxygen absorption decreases[83,88]. The introduction of hydrogen peroxide considerably accelerates the rate of depolymerisation during oxidation by molecular oxygen both of alkaline cellulose[104-106] and of a cellulose suspension[107]; the rate of depolymerisation increases with increase in the hydrogen peroxide concentration. Additions to cellulose of sodium sulphide[104], sodium hypochlorite[104,108], and ammonium persulphate (in amounts of 1–8%)[104] accelerate the depolymerisation of alkaline cellulose. The presence in the impregnating alkali of 1% of substances capable of autoxidation, such as glucose and sodium dithionite, has little effect on the rate of depolymerisation of cellulose.

(*c*) Change in functional groups during oxidation of cellulose

An important feature of the oxidation of cellulose is the formation of carbonyl and carboxyl groups in the macromolecules.

According to Davidson[83] and to Entwistle et al.[84] the reducing power of cellulose, as measured by the copper number, increases continuously during the oxidation of alkaline cellulose by molecular oxygen. According to other workers[81,94,109] the reducing power increases only during the first few hours of oxidation, after which it remains almost unchanged. For a given oxygen absorption the content of aldehyde groups is larger with higher alkali concentrations and in the presence of oxidation catalysts[83,88]. Only a slight change in copper number was observed[97] during the oxidation of a suspension of cellulose.

Both aldehydic and ketonic groups are formed in the oxidation of alkaline cellulose[77]. It is not surprising that the reducing power of cellulose observed during oxidation is slight, since in alkaline media the carbonyl groups undergo further oxidation or the other reactions described earlier. The content of carboxy-groups gradually increases with increasing duration of oxidation[81,84,88,109,110]. At a given oxygen absorption the carboxyl content is greater in the presence of cobalt[88].

The oxidation of alkaline cellulose by molecular oxygen involves the formation of peroxides[84,99,111], the quantity of which diminishes in the presence of traces of salts of metals that catalyse oxidation (cobalt, manganese) and also metals that inhibit oxidation (silver). No peroxide at all could be detected in the presence of 0.0006% of cobalt or 0.0032% of silver[84,88].

(*d*) Chemical composition of products of the oxidative–alkaline degradation of cellulose

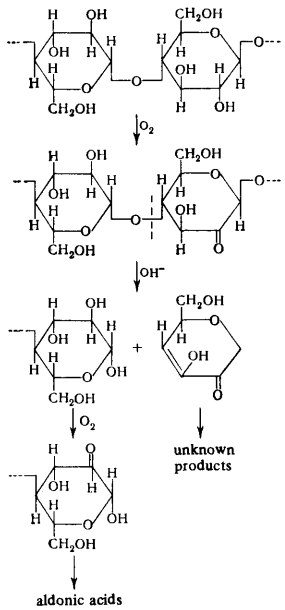
Examination of the changes in functional groups and degree of polymerisation during oxidation by molecular oxygen still does not provide an accurate idea of the chemical changes undergone by the cellulose molecule. It is true that the fact that a small quantity of absorbed oxygen produces a considerable change in degree of polymerisation indicates that oxidation occurs throughout the length of the cellulose molecule, not only at its ends. It was suggested that oxygen would attack preferentially carbon atoms carrying the most ionised hydroxy-groups, i.e. the second carbon atom in the repeating unit[84].

However, a more exact picture of the reaction mechanism can be obtained only from a study of the structure of the oxidation products—both those of low molecular weight, which pass into solution, and those of high molecular weight, remaining in the solid phase.

The chemical composition of cellulose remaining after oxidation with molecular oxygen in an alkaline medium depends on the conditions. The only acid found after the oxidation of cellulose hydrate suspended in 1% caustic soda solution in air at 100°C was erythronic acid [112]. Arabonic acid was found, with smaller quantities of erythronic and mannonic acids, in the oxidised cellulose formed from alkaline cellulose at 33°C; small quantities of gluconic and ribonic acids were also detected [113].

According to a hypothetical scheme to explain the formation on erythronic acid [112] the main reaction involves oxidation of the secondary alcoholic groups at $C_{(2)}$ and $C_{(3)}$ to keto-groups with subsequent oxidation to the dicarboxylic acid, which in turn is oxidised to a carbonic ester. Hydrolysis of the ester in an alkaline medium results in cleavage of the macromolecules to give an erythronic acid residue at the end of one newly formed cellulose molecule, and a non-reducing anhydroglucose unit at the end of the other molecule [112].

Scheme 2



Another series of reactions (Scheme 2) has been suggested for the oxidative degradation of alkaline cellulose by workers [113] who found that the oxidised cellulose contained as terminal units arabonic, erythronic, mallonic, gluconic, and ribonic acids in roughly the same proportions as are formed in the oxidation of glucose and cellobiose under similar conditions [114]. On the basis of this observation it was suggested [113] that the terminal aldonic-acid units were formed by the oxidation of reducing terminal glucose units in the cellulose.

2. Mechanism of the Oxidation of Cellulose by Molecular Oxygen in Alkaline Media

(*a*) Radical-chain mechanism of the oxidation of cellulose

During the past two decades investigators have begun to work on elucidating the mechanism of the oxidation of cellulose by molecular oxygen in alkaline media. The first papers on this problem were published in 1949 by Entwistle, Cole, and Wooding [84,88], who suggested a radical-chain mechanism analogous to that of the autoxidation of alkenes. They based it on kinetic data on the absorption of oxygen by alkaline cellulose during oxidation, observations on the catalytic action of transition-metal ions, inhibition by silver and organic antioxidants, the increase in the initial rate of oxidation on the addition of substances that dissociate to form free radicals, and the relation between the initial rate of oxidation and the content of reducing groups. This mechanism includes the stages indicated in the subheadings below.

Chain initiation. The autoxidation of alkaline cellulose begins by the detachment of an active hydrogen atom by molecular oxygen. In cellulose the hydrogen of an aldehyde group (perhaps enolised) is active:

$$R_{cell}-\underset{\underset{H}{|}}{\overset{\overset{O}{\|}}{C}} + O_2 \rightarrow HOO^{\cdot} + R_{cell}-C^{\cdot}=O \quad (1)$$

The resulting cellulose radical then reacts as follows:

$$R_{cell}-C^{\cdot}=O + O_2 \rightarrow R_{cell}-CO(OO^{\cdot}) \quad (2)$$

$$R_{cell}-CO(OO^{\cdot}) + R_{cell}-H \rightarrow R_{cell}-CO(OH) + R^{\cdot}_{cell} \quad (3)$$

Entwistle and his coworkers put forward the hypothesis that the allylic hydrogen in an enolised reducing thermal unit of cellulose should be especially labile, and removable by molecular oxygen:

$$R_{cell}-\underset{\underset{CH_2OH}{|}}{\overset{\overset{CHOH}{|}}{OCH-CHOH-C(OH)=CHO^-}} \xrightarrow{+O_2} R_{cell}-\underset{\underset{CH_2OH}{|}}{\overset{\overset{CHOH}{|}}{OCH-\dot{C}(OH)-C(OH)=CHO^-}} + HOO^{\cdot}$$

These workers assume [84] that oxidation is facilitated by ionisation of the hydroxy-groups of cellulose. The presence of an ionised hydroxyl on a carbon atom attached to hydrogen may strongly polarise and weaken the carbon-hydrogen bond. Oxidising attack in an unchanged repeating unit of cellulose probably takes place at the carbon atom having the most ionised hydroxyl, and hence primarily at the second carbon atom of the anhydroglucose unit.

Chain propagation. Subsequent oxidation of the cellulose takes place by alternation of the reactions

$$R^{\cdot}_{cell} + O_2 \rightarrow R_{cell}-OO^{\cdot} \quad (4)$$

$$R_{cell}-OO^{\cdot} + R_{cell}-H \rightarrow R_{cell}-OOH + R^{\cdot}_{cell} \quad (5)$$

and the hydroperoxy-radical detaches a hydrogen atom from a carbon atom of a repeating unit. In an alkaline medium the resulting hydroperoxides are usually hydrolysed to form hydrogen peroxide:

$$R_{cell}-OOH + H_2O \rightarrow R_{cell}-OH + H_2O_2 \quad (6)$$

After the hydrolysis of hydroperoxides formed on the second, third, or sixth carbon atom of the repeating unit, hydrated forms of the ketone or aldehyde are produced, which immediately lose water to give a keto- or aldehydo-cellulose. If the hydroperoxide has been formed on the

fourth or fifth carbon atom, hydrolysis yields a hemiacetal, which is rapidly hydrolysed with cleavage of the cellulose molecule. Hydrolysis of a hydroperoxide on the first carbon atom produces an orthoester, which in an alkaline medium is also rapidly hydrolysed with rupture of the chain.

The hydroperoxide formed may also undergo homolytic decomposition to give a free radical on the cellulose and a free hydroxy-radical, so that chain branching occurs:

$$R_{cell}\cdot OOH \rightarrow R_{cell}-O^{\cdot} + HO^{\cdot}. \qquad (7)$$

Homolytic decomposition of hydroperoxides is accelerated in the presence of catalytically active metals:

$$R_{cell}-OOH + M^{2+} \rightarrow R_{cell}-O^{\cdot} + HO^{-} + M^{3+}. \qquad (8)$$

Thus the catalytic effect of metals emphasises the radical-chain character of the reaction, although oxidation may take place in their absence. When transition-metal ions are not present, a cellulose hydroperoxide will break down mainly with the liberation of hydrogen peroxide by reaction (6).

Chain termination. Termination may be caused by the association of radicals or by the reaction of radicals with impurities. Since alcohols and carbohydrates can be active inhibitors of chain reactions, it was assumed [84] that the reaction chains might be relatively short.

A weighty argument in favour of the formation of free radicals in the macromolecule in the oxidation of alkaline cellulose is Schurz's observation of the formation of a graft copolymer by the action of styrene on the spontaneously oxidising alkaline cellulose system: a homopolymer is not formed. However, the life of the radicals is very brief, especially at high temperatures. In this worker's opinion the long-lived groups initiating the graft copolymerisation after oxidation has ceased are peroxy-groups in the cellulose, which on heating give free radicals [115]. However, Mottor's attempts to detect free radicals by electron spin resonance were unsuccessful [116]. Determination of the quantity of hydroxyl radicals by a chemical method based on the convertion of benzene into phenol showed their almost complete absence.

(*b*) Ionic mechanism for the oxidation of cellulose

In view of his finding that hydroxyl radicals are absent, Mottor assumes [116] that the autoxidation of alkaline cellulose takes place by an ionic mechanism. Oxygen is regarded as reacting initially with reducing functional groups in the cellulose, probably aldehyde groups, which in an alkaline medium behave as Lewis acids and form the anions (XX) and (XXI):

$$R_{cell}-\underset{\underset{H}{\diagdown}}{\overset{\overset{O}{\diagup}}{C}} \underset{\rightleftharpoons}{\overset{HO^-}{\rightarrow}} R_{cell}-\underset{OH}{\overset{O^-}{\underset{\diagdown}{\overset{\diagup}{C}}}}-H \underset{\rightleftharpoons}{\overset{HO^-}{\rightarrow}} R_{cell}-\underset{O^-}{\overset{O^-}{\underset{\diagdown}{\overset{\diagup}{C}}}}-H + H_2O \quad . \qquad (9)$$

(XX) (XXI)

These anions are able to donate a hydride ion to an oxygen molecule to form a hydrogen peroxide ion:

$$R_{cell}-\underset{O^-}{\overset{O^-}{\underset{\diagdown}{\overset{\diagup}{C}}}}-H + O_2 \rightarrow R_{cell}-\underset{O^-}{\overset{O}{\underset{\diagdown}{\overset{\diagup}{C}}}} + HOO^-, \qquad (10)$$

which oxidises the cellulose.

The ability of hydrogen peroxide to oxidise cellulose is well known [105,117,118]. Kleinert showed that the changes occurring in the oxidation of alkaline cellulose are analogous to those accompanying the oxidation of cellulose by hydrogen peroxide in 18% caustic soda [105].

(*c*) Ion–radical chain mechanism for the oxidation of cellulose

MacDonald [107] combined the two views on the autoxidation of alkaline cellulose and suggested that the initial stages take place by an ionic mechanism, and later stages by a radical mechanism. On the basis of Mottor's results showing the absence of hydroxyl or perhydroxyl radicals during the autoxidation of alkaline cellulose, those of other workers on the effect of transition-metal ions on the formation of hydrogen peroxide and the fall in the viscosity of cellulose, and also his own results on the inhibition of autoxidation by sulphur and on the quantity of hydrogen peroxide formed during the autoxidation of cellulose suspended in caustic soda solution [107], MacDonald considers that at the start of the process, when the reducing groups of the cellulose are undergoing oxidation, hydrogen peroxide can be formed only by Mottor's ionic mechanism (reactions 9 and 10). In the presence of metal catalysts the resulting hydrogen peroxide would form cellulose free radicals but not hydroxyl or perhydroxyl radicals. MacDonald considers that the cellulose radicals are formed by detachment of a hydrogen atom from cellulose by means of complexes of hydrogen peroxide ions with tervalent iron ion. Such complexes had been described by Kremer in a study of the decomposition of hydrogen peroxide by iron(III) salts [119]. The cellulose radicals then react by the chain mechanism suggested by Entwistle et al. (reactions 4–6). The oxidation products $R_{cell}OH$ undergo the further reactions described earlier.

A rather different mechanism was suggested by Michie and Neale [86] for the oxidation of cellulose in an alkaline medium. On the basis of their kinetic data on the absorption of oxygen by cellulose suspended in caustic soda solution, and also data obtained by other investigators on the autoxidation of alkaline cellulose, glucose, and α-ketols, they considered direct initiation of autoxidation by radicals formed by interaction between oxygen and reducing groups in the cellulose to be impossible. They assumed that initiation is effected by monomeric radicals formed by decomposition of hydroperoxides, the latter produced by the reducing groups at the start of the process. Transition-metal ions play an important part in the decomposition of the hydroperoxides. Oxidation then proceeds as in most cases of autoxidation. Formation of a cellulose radical is followed by absorption of oxygen with formation of the corresponding peroxy-radical. The latter radical would be extremely unstable, because hydroperoxides are hydrolysed rapidly in alkaline solution, and also because of the instability of compounds containing a peroxy- and a hydroxy-group attached to the same carbon atom. This radical may therefore be expected to break down rapidly to give an $HO_2^{\cdot}$ radical and a carbonyl group. Under alkaline conditions the $HO_2^{\cdot}$ radical will be almost completely dissociated into the radical ion $O_2^{\cdot -}$. The hydroperoxy-radical $HO_2^{\cdot}$ is known to be far less reactive than the hydroxyl radical $HO^{\cdot}$, [120] so that the ionised form of the former radical will probably be a still weaker oxidising agent. But these workers consider that the radical ion $O_2^{\cdot -}$ is nevertheless able to oxidise a cellulose molecule ionised in strongly alkaline medium.

Michie and Neale give the following scheme for the oxidation of cellulose:

(i) chain initiation

$$HO_2^- \rightarrow O_2^- \quad , \tag{11}$$

(ii) chain propagation

$$O_2^- + R_{cell}\text{—}\overset{|}{C}HO^- \rightarrow R_{cell}\text{—}\overset{|}{C}\cdot\text{—}O^- + HO_2^- \tag{12}$$

$$R_{cell}\text{—}\overset{|}{C}\cdot\text{—}O^- + O_2 \rightarrow R_{cell}\text{—}\overset{|}{C}\text{=}O + O_2^- \quad , \tag{13}$$

(iii) chain termination

$$R_{cell}\text{—}\overset{|}{C}\cdot\text{—}O^- + O_2^-(H^+) \rightarrow R_{cell}\text{—}\overset{|}{C}\text{=}O + HO_2 \quad . \tag{14}$$

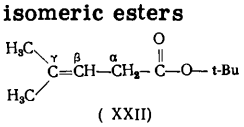
$$2\,O_2^- + H^+ \rightarrow HO_2^- + O_2 \tag{15}$$

Ionisation of the hydroxy-groups of cellulose and of a cellulose radical are represented by the equations

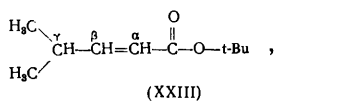
$$R_{cell}\text{—}\overset{|}{C}HOH + HO^- \rightarrow R_{cell}\text{—}\overset{|}{C}HO^- + H_2O \tag{16}$$

$$R_{cell}\text{—}\overset{|}{C}\cdot OH + HO^- \rightarrow R_{cell}\text{—}\overset{|}{C}\cdot\text{—}O^- + H_2O \quad . \tag{17}$$

Thus no generally accepted view has yet emerged on the mechanism of the oxidation of cellulose by molecular oxygen in alkaline media, as on the mechanism of the oxidation under analogous conditions of many compounds of low molecular weight. It may be supposed that, besides the above possible mechanisms of oxidation, some part in these processes will be played by the reactions of carbanions formed under the influence of the alkali. A basis for such a hypothesis is provided by data on the oxidation of esters and ketones in alkaline media with the formation of α-hydroxyperoxides [121,122]. This possibility is demonstrated still more clearly by results for the oxidation of the isomeric esters



(XXII)



(XXIII)

which in an alkaline medium give a considerable quantity of α-oxidised products, but only γ-hydroperoxides by true free-radical oxidation in benzene solution [123].

One possible oxidation mechanism involving carbanions is represented by the scheme [124-127]

$$\rangle C^- + O_2 \rightarrow \rangle C\cdot + O_2^- \tag{18}$$

$$\rangle C\cdot + O_2 \rightarrow \rangle COO\cdot \tag{19}$$

$$\rangle COO\cdot + \rangle C^- \rightarrow \rangle COO^- + \rangle C\cdot \quad . \tag{20}$$

In the classical free-radical mechanism of oxidation, initiation is effected by the detachment of a hydrogen atom from the oxidisable compound (e.g. Eqn. 1), but in the present case it occurs by electron transfer (Eqn. 18). If such a mechanism is accepted, the great ease of oxidation in the presence of alkalis compared with oxidation in neutral medium can be explained. Another mechanism is also possible for the oxidation of carbanions:

$$\rangle C^- + O_2 \rightarrow \rangle CO_2^- \quad . \tag{21}$$

However, there are grounds for thinking that this process is improbable [128].

Whatever the mechanism of oxidation, its result is always the formation of hydroperoxides (or hydroperoxy-radicals) as reaction intermediates. In alkaline media the hydroperoxides are hydrolysed with the formation of hydrogen peroxide, which is able to oxidise cellulose. Further support for this is given by Müller's results [99] showing that the degree of polymerisation of cellulose remains completely unchanged when alkaline cellulose is oxidised by molecular oxygen in the absence of water, whereas with an insufficient quantity of water it changes more slowly than during the oxidation of cellulose in the presence of a sufficient quantity. The absence of water probably slows down not only the rate of formation of hydroperoxides, owing to the diminished degree of ionisation of the cellulose hydroxyls, but also terminates the formation of hydrogen peroxide, because of the impossibility of the hydrolysis of hydroperoxides under anhydrous conditions.

Unfortunately, the mechanism of oxidation by hydrogen peroxide in an alkaline medium has not yet been accurately established. Most investigators adhere to a radical reaction mechanism: they consider that the active oxidising agent is the hydroxyl radical, formed by the decomposition of hydrogen peroxide in the alkaline medium. Kazarnovskii and Neiding [129] assume that the decomposition of hydrogen peroxide in alkaline solutions is caused by reaction between products of its electolytic dissociation and the undissociated molecules:

$$\left.\begin{aligned} H_2O_2 &= H^+ + HO_2^- \\ HO_2^- &= H^+ + O_2^{2-} \end{aligned}\right\} \text{electrolytic dissocation}$$

$$O_2^{2-} + H_2O_2 = O_2^- + OH^- + OH\cdot \quad \text{(chain initiation)}$$

$$\left.\begin{aligned} H_2O_2 + OH\cdot &= H_2O + HO_2\cdot \\ HO_2\cdot &= H^+ + O_2^- \\ H_2O_2 + O_2^- &= OH^- + O_2 + OH\cdot \end{aligned}\right\} \text{reaction chain} \quad .$$

Several investigators, however, hold a different view on the mechanism of the oxidising action of hydrogen peroxide, regarding the active agent as the anion HO_2^-. [130-132]

It must be supposed that further investigations on the mechanism of the oxidative-alkaline breakdown of cellulose under the influence of molecular oxygen in various media will establish the actual mechanism of these processes.

IV. EFFECT OF SUPERMOLECULAR STRUCTURE OF CELLULOSE ON ITS ALKALINE AND OXIDATIVE-ALKALINE DEGRADATION

The reactivity of cellulose, as of other biopolymers, is greatly dependent on its supermolecular structure. The ordered "crystalline" portions of cellulose must be supposed to be less reactive than the disordered "amorphous" portions, which are more easily accessible to chemical reagents. Structure may affect both the rate of depolymerisation and the nature of the processes involved, by changing the relative reactivities of atoms and groups in the repeating unit.

Few data are available on the effect of the supermolecular structure on alkaline degradation, but they are consistent with the above view. Thus Meller [133] noted the effect of the structure of the cellulose fibre on the rate of the changes occurring from the reducing end, and suggested [4,133] that intramolecular and intermolecular hydrogen bonds play a part in the reactivity of celluloses.

Colbran and Davidson [12] showed that hydrocelluloses obtained from mercerised cotton cellulose are more stable to the action of hot dilute alkalis than are those obtained from unmercerised cotton cellulose of the same reducing power. The alkali-insoluble cellulose had considerably lower copper numbers and contained a greater quantity of carboxy-groups in the case of degradation of the hydrocelluloses obtained from mercerised cellulose.

The difference was explained by the effect of the supermolecular structure on the stabilising reaction, which is evidently favoured by the structure of cellulose II. Evidence of the greater resistance of this form to hot dilute alkalis is provided also by Machell and Richards' results [134] showing that pretreatment of hydrocellulose with 5 *N* sodium hydroxide solution increases its stability to the subsequent action of the 0.5 *N* alkalis at 100°C and by the enhanced stability [135] of unbleached sulphite pulp to the action of hot dilute alkalis resulting from its mercerisation.

Swelling and "decrystallisation" of cellulose diminish its resistance to hot dilute alkalis [133].

Machell and Richards [134] and Colbran and Davidson [12] observed that only certain molecules in the residue resistant to further degradation, obtained when hydrocellulose was treated with hot dilute alkali, contained metasaccharinic acid as terminal unit. These workers assumed that degradation ceased not only when the reducing terminal unit of cellulose was converted into a metasaccharinic acid residue but also when the reactant end of the molecule reached inaccessible (crystalline) regions of the cellulose fibre. Richtzenhain et al. [10] found no significant differences in the X-ray patterns or in the distribution curves for the degree of polymerisation of hydrocellulose before and after treatment with hot dilute alkali. The explanation offered was that only that part of the material located in disordered regions and on the surface of ordered regions of the cellulose suffered breakdown.

Very few results have been published on the effect of the supermolecular structure of cellulose on its oxidation by molecular oxygen in alkaline media. However, the available data indicate that the less ordered portions of cellulose are the more reactive. Thus the rate of oxidation of alkaline cellulose is considerably increased if the cellulose has first been swollen in alkali [83,99]. The X-ray patterns of cellulose oxidised after swelling are typical of cellulose hydrate, whereas the interference pattern obtained after oxidation without preliminary swelling is identical with that of native cellulose [99]. Preswelling obviously increases the proportion of amorphous regions in the supermolecular structure. As Brassard suggested [100], this process may be responsible for the increase in the rate of oxidation of alkaline cellulose with increase in the caustic soda concentration (see Section III, 1*b*).

A fairly recent investigation [136] of the effect of the supermolecular structure of cellulose on its oxidative degradation by the action of molecular oxygen on a suspension in 1% caustic soda solution at 100°C has shown a marked difference in rate of oxidation between natural cotton cellulose and cellulose hydrate obtained from cotton cellulose. After the carbonyl groups had been reduced, the hydrate was degraded at a greater rate, whereas natural cotton cellulose underwent only slight degradation. The structure of cellulose hydrate differs from that of natural cotton cellulose in the type of packing of molecules in the ordered ("crystalline") regions, in the size of the densely packed regions, and in the degree of ordering (crystallinity) of the cellulose. The influence of these structural features on the rate of oxidative-alkaline degradation was investigated.

This work showed that, after the carbonyl groups had been reduced, oxidative-alkaline degradation occurred at the same rate in densely packed regions of native cotton cellulose and in the cellulose hydrates isolated from them by hydrolysis. Thus the difference in the rates of oxidation of the two materials can be explained only by different degrees of ordering, which was confirmed by examining the oxidation of specimens of cellulose differing in this parameter. It should be mentioned in this connection that cellulose undergoes oxidation even in the absence of carbonyl groups [136]. Cellulose hydrate, which X-ray examination showed to possess a lower degree of ordering, is then oxidised especially intensely. It was concluded from the experimental results that the oxidising process can be initiated not only by carbonyl groups but also by hydroxyls situated in disordered regions.

The constancy of the degree of polymerisation during the oxidation of hydrocelluloses, obtained both from native cotton cellulose and from cellulose hydrate, implies [136] that the oxidative-alkaline degradation of hydrocelluloses takes place only from the ends of macromolecules and on the surface of ordered regions.

The above survey of the literature shows that processes involved in the degradation of the cellulose molecule and oxidised celluloses have been studied in detail, whereas the reaction mechanism of the oxidation of cellulose by molecular oxygen in an alkaline medium had not yet been adequately elucidated. These processes are of the utmost importance in the technology of cellulose and other polysaccharides, and further research is needed in order to control them.

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Zelinskii Institute of Organic Chemistry,
USSR Academy of Sciences,
Moscow

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Dynamic Nuclear Magnetic Resonance

N.M.Sergeev

Nuclear magnetic resonance spectroscopy has been widely used in recent years to investigate the kinetics of chemical reactions. Dynamic nuclear magnetic resonance spectroscopy covers the investigation of temperature-dependent n.m.r. spectra and the calculation of rate constants and Arrhenius parameters from these spectra. The present Review describes the principles of d.n.m.r. spectroscopy, methods of recording the spectra, and their processing by exact and approximate methods. The theoretical and experimental foundations are illustrated by many examples of the investigation of hindered rotations, inversions, and rearrangements in various organic and organometallic systems. A list of 81 references is included.

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I. INTRODUCTION

The most diverse physicochemical methods have been used to investigate the kinetics of chemical reactions[1-4]. Recently nuclear magnetic resonance (n.m.r.) spectroscopy has found wide application. Dynamic nuclear magnetic resonance (d.n.m.r.) spectroscopy involves observing the changes with temperature in n.m.r. spectra and hence calculating reaction rate constants and the corresponding Arrhenius parameters. Dynamic effects in n.m.r. spectra were first detected by Gutowsky and his coworkers in 1953.[5,6] Since then various investigations have been made in this field, and several reviews have been published[7-13] on the theory and applications of d.n.m.r. spectroscopy.

At the present stage in the development of the technique and applications of d.n.m.r. spectroscopy several new and original methodological principles have been suggested which broaden significantly the possibilities, and among which carbon-13 n.m.r. spectroscopy may be the most promising approach. Secondly, the abundance of experimental data and the inadequacy of procedures for their analysis demand a critical assessment of the accuracy with which activation parameters are measured. Thirdly, the application of d.n.m.r. has led to the discovery of a completely new class of fluctuating or stereochemically non-rigid molecules, i.e. compounds capable of degenerate intramolecular rearrangements. The present Review discusses these problems as illustrated by various organic and organometallic systems.

II. ELEMENTS OF THE THEORY OF DYNAMIC NUCLEAR MAGNETIC RESONANCE

Dynamic n.m.r. data are usually analysed in terms of the theory of rate processes, clear and detailed accounts of which can be found in monographs[3,4]. Only the main formulae are given below.

The reaction A ⇌ B can be represented most simply by a plot of free energy against the generalised reaction coordinate (Fig. 1), where the state of maximum energy is termed the transition state (Tr). The rate constant of the change from state A to state B is given by the formula

$$k_{AB} = \varkappa \frac{k_{Bol}T}{h} \exp(-\Delta G^{\neq}_{AB}/RT) , \quad (1a)$$

$$\Delta G^{\neq}_{AB} = \Delta H^{\neq}_{AB} - T\Delta S^{\neq}_{AB} , \quad (1b)$$

where $\varkappa$ is the transmission coefficient, $\Delta S^{\neq}$, $\Delta H^{\neq}$, and $\Delta G^{\neq}$ are the entropy, enthalpy, and free energy of activation respectively, T is the temperature, and the remaining symbols represent fundamental constants. In view of the slight temperature dependence of the pre-exponential factor, use is often made of the Arrhenius equation

$$k = A \cdot \exp(-E_a/RT) , \quad (2)$$

where A is the frequency factor and E_a is the activation energy. Comparison of Eqns. (1) and (2) gives

$$\Delta H^{\neq} = E_a - RT ,$$

$$\Delta G^{\neq} = E_a - RT - T\Delta S^{\neq} , \quad (3)$$

$$A = \varkappa \frac{k_{Bol}T}{h} \cdot e \cdot \exp(\Delta S^{\neq}/RT) .$$

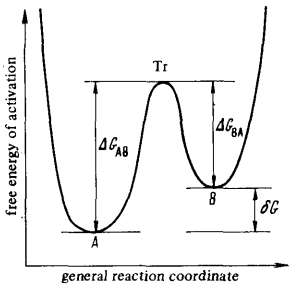


Figure 1. Form of potential-energy surface for exchange between two states.

The activation energy is determined experimentally from the dependence of $\ln k$ on $1/T$ by means of the equation

$$E_a = -R \cdot \frac{\partial(\ln k)}{\partial(1/T)} . \quad (4)$$

Under equilibrium conditions we can determine the equilibrium constant for the reaction A ⇌ B

$$K = p_A/p_B = k_B/k_A = \exp(-\delta G/RT) , \quad (5)$$

where p_A and p_B are the populations (or concentrations) of states A and B, and $\delta G = \Delta G^{\neq}_{AB} - \Delta G^{\neq}_{BA}$.

If the reaction rate constant k_{AB} is considerably smaller than 0.01 s^{-1}, the reaction is slow. The n.m.r. method can then be used to monitor the changes in concentration of the states with time by measuring the integral intensities of the corresponding signals. In spite of the triviality of such measurements, there are an immense number of examples where n.m.r. is used in this way, including extremely complicated coupled reactions in multicomponent systems. Several examples can be found in Ionin and Ershov's book[13].

The concept of the lifetime τ of a state[11-13] is often used in d.n.m.r. spectroscopy. For complex reactions the lifetime τ_{ij} of a state i with respect to transition to state j is defined by the formula

$$\tau_{ij} = 1/k_{ij} . \quad (6)$$

The lifetime may vary within wide limits depending on the temperature (Eqns. 1 and 2). The choice of method for recording a rate process is determined by the ratio of the lifetime of the state to the characteristic time of the method τ_m. The latter quantity is a time constant characterising the processes of energy dissipation (relaxation) in the corresponding frequency range (Table 1). Intermittent processes in a molecular system that are more rapid than the dissipation (relaxation) processes in the corresponding frequency range cannot be recorded, and such a system appears static (averaged over the states involved) when the given method is used.

Table 1. Characteristic times of some physical methods used in chemistry.

Method	Time, s	Method	Time, s
Electron diffraction	10^{-20}	Electron spin resonance	10^{-4}—10^{-8}
X-Ray diffraction	10^{-18}	Nuclear magnetic resonance	10^{-1}—10^{-7}
Ultraviolet (electronic) spectra	10^{-14}—10^{-15}	Molecular beams	10^{-6}
Vibrational spectra	10^{-11}—10^{-13}	Visual methods (separation of isomers)	10^{2}
Ultrasonic absorption	10^{-5}—10^{-9}		

It is interesting that the characteristic time constant of the n.m.r. method covers a very wide range (Table 1). The reason is that various methods are used in n.m.r. spectroscopy, which permit the recording of processes ranging from rapid ($k \simeq 10$ s^{-1}) to very rapid ($k \simeq 10^7$ s^{-1}). This range of reaction velocities is usually inaccessible to other methods[12-15]—a fact responsible for the widespread interest in d.n.m.r. spectroscopy.

The discovery of dynamic effects on n.m.r. spectra[5,16] was followed by theoretical descriptions of this phenomenon by Gutowsky and Holm[16], Hahn and Maxwell[17], and McConnell[18] based on Bloch's phenomenological equations for the nuclear magnetisation vector[19]. This work has been analysed in reviews[7,8], so that we shall merely give the equation for the complex magnetisation G in exchange between two positions A ⇌ B

$$G = i\omega_1 M_0 \frac{[(\tau_A + \tau_B) + \tau_A\tau_B(\alpha_A p_A + \alpha_B p_B)]}{(1+\alpha_A\tau_A)(1+\alpha_B\tau_B)} \quad (7)$$

where $\omega_1 = \gamma H_1$ (in which γ is the gyromagnetic constant and H_1 the amplitude of the high-frequency field), M_0 is the equilibrium intensity of magnetisation,

$$\alpha_i = \frac{1}{T_2} + i(\omega_i - \omega)$$

τ_A and τ_B are the lifetimes in states A and B,

$$p_A = \frac{\tau_A}{\tau_A + \tau_B} , \qquad p_B = \frac{\tau_B}{\tau_A + \tau_B} , \quad (8a)$$

$$\tau = p_A\tau_B = p_B\tau_A . \quad (8b)$$

T_2 is the spin–spin relaxation time, and ω_i and ω are the resonance and instantaneous frequencies respectively.

The complex magnetisation G is defined as $u + iv$, where in particular the component v perpendicular to the field vector H_1 is termed the absorption signal[7,11,12,19], while the component u is the dispersion signal. The v components are usually recorded. The form of the absorption signal for a two-position exchange can be obtained from the imaginary part of Eqn. (7):

$$v = \omega_1 M_0 \frac{[(1+\tau/T_2)P + QR]}{P^2 + R^2} \qquad (9)$$

where

$$P = \tau\left\{\frac{1}{T_2^2} = \left[\frac{1}{2}(\omega_A + \omega_B) - \omega\right]^2 + \frac{1}{4}(\omega_A - \omega_B)^2\right\} + \frac{1}{T_2} ,$$

$$Q = \tau\left\{\frac{1}{2}(\omega_A + \omega_B) - \omega - \frac{1}{2}(\omega_A - \omega_B)(p_A - p_B)\right\} ,$$

$$R = \left\{\frac{1}{2}(\omega_A + \omega_B) - \omega\right\}(1 + 2\tau/T_2) + \frac{1}{2}(\omega_A - \omega_B)(p_A - p_B).$$

Analysis of Eqn. (9) enables two regions of values of τ to be isolated, for which quite accurate calculations can be made by means of simplified formulae[16,18].

1. Approximation of Slow Exchange $\tau \gg (\nu_A - \nu_B)^{-1}$†

Two signals are observed corresponding to the two states with their statistical weights p_A and p_B. The signal from A in particular has a Lorenzian profile, and the line width $\delta\nu_A$ (in c/s) at midheight is given by

$$\delta\nu_A = \frac{1}{\pi T_{2A}} + \frac{1}{\pi\tau_A} \quad . \qquad (10)$$

2. Approximation of Rapid Exchange $\tau \ll (\nu_A - \nu_B)^{-1}$

Only one signal is observed, having the resonance frequency $\nu = p_A\nu_A + p_B\nu_B$. Its width is given approximately by Meiboom's formula[20]

$$\delta\nu = \frac{p_A}{\pi T_{2A}} + \frac{p_B}{\pi T_{2B}} + 4\pi^2 p_A^2 p_B^2 (\nu_A - \nu_B)^2(\tau_A + \tau_B) \quad . \qquad (11)$$

Computers are generally employed to calculate the complete line shape of the signal of the v component for any values of τ_A and τ_B, owing to the cumbersome computations involved, although a few other approximate methods have been suggested (nomograms[12,21], ratio of maxima and minima in the absorption spectrum[22]).

Fig. 2 illustrates the changes undergone by the spectrum in a two-position exchange. When the populations of the states are equal $p_A = p_B = \frac{1}{2}$, the separate stages in the dynamic process are easily detected. When $\tau >$ 100 s, no appreciable broadening of the lines is observed, and exchange cannot be detected. With slow exchange $\tau \simeq 1$ s, each component of the spectrum becomes wider and moves towards the centre (Fig. 2*a*). The signals coalesce at values of $\tau = \sqrt{2}/2\pi(\nu_A - \nu_B)$. On subsequent increase in the rate of exchange the line again narrows. Finally, with $\tau < 10^{-5}$ s (with $\Delta\nu = 100$ Hz—Eqn. 11), the broadening becomes so small ($\sim$ 0.1 c/s) that the exchange process can no longer be reliably recorded. Exchange effects are similar in the case of unequal populations (Fig. 2*b*), the only difference being that they are more significant for the less populated state (B in Fig. 2*b*). It is easily seen that, if the difference in free energies δG exceeds 3 kcal mole^{-1} (Fig. 1), which corresponds to $p_B < 10^{-2}$, the exchange effects become so small that it becomes difficult to record the actual fact of exchange.

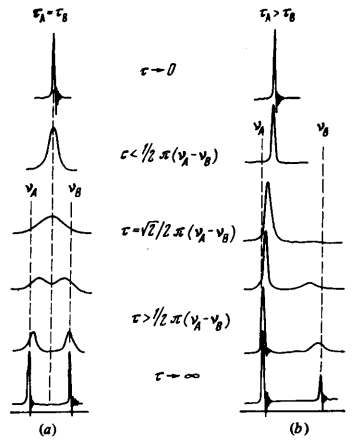


Figure 2. Qualitative shapes of n.m.r. signals for two-position exchange with spectra obtained under the conditions: a) $\tau_A = \tau_B$; b) $\tau_A \neq \tau_B$.

These conditions impose evident limits to the applicability of the d.n.m.r. method to the investigation of rate processes.

III. TECHNIQUE FOR THE ANALYSIS OF DYNAMIC NUCLEAR MAGNETIC RESONANCE SPECTRA

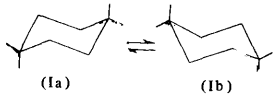
In practice the dynamic effects in n.m.r. spectra described in Section II are always complicated by several additional factors. The greatest difficulties arise from the multiplet structure of the spectra due to indirect spin–spin interaction, in which two cases must be distinguished. (i) The n.m.r. spectra for weakly coupled spin systems ‡ can be regarded as a superposition of d.n.m.r. spectra analogous to those shown in Figs. 2*a* and 2*b* for $p_A = p_B$ and $p_A \neq p_B$ respectively. Simple graphical methods of calculating rate constants have been developed[24,25] to analyse multiplet d.n.m.r. spectra. Relations have also been suggested[26,27] enabling several more complicated situations to be analysed, in which methods of subspectral analysis make it possible to isolate simple subspectra. (ii) With strongly coupled spin systems a complete description of the high-resolution spectra is impossible on the basis of the Bloch equations, and methods of quantum mechanics must be used. A complete description of the effects in systems with strong coupling of the spins was first given by Kaplan[28] using the

† Here and subsequently it is convenient to use angular frequencies $\nu = \omega/2\pi$.

‡ This term is applied to systems[23] in which any pair of nuclei with resonance frequencies ν_A and ν_B and a spin–spin interaction constant J_{AB} conforms to the relation $J_{AB}|\nu_A - \nu_B| \ll 1$.

density matrix. This method was later developed by Alexander[29] for the interchange of spins. Work on these lines was reviewed by Johnson[8] and by Lynden-Bell[9]. In recent years Binsch has put forward a general theory of line shape in high-resolution n.m.r. spectra based on Liouville's theorem[30,31].

The multiplet character of the signals in d.n.m.r. spectra must be taken into account because the most widely used method for analysing dynamic effects is proton magnetic resonance (p.m.r.) spectroscopy[12,13]. The investigation of inversion in cyclohexane



provides a typical example of the procedure for allowing for such multiplets[11-13,32-37]. At room temperature the p.m.r. spectrum is a narrow singlet, so that cyclohexane can be used as a standard of resolution. As the temperature falls the signal begins to broaden, and at −50°C its width is ~ 20 Hz (for a proton resonance frequency of 60 MHz [32]). With further drop in temperature the signal divides into two multiplets separated by 0.5 ppm and having a complicated structure[32]. Below −100°C the width of the lines of the doublet is maintained. The changes observed in the spectrum are interpreted as due to inversion of the ring (Ia ⇌ Ib). With such inversion each proton is sometimes in an axial position and sometimes in an equatorial position: i.e. it is "exchanged" between the two positions.

One of the most important stages in the investigation of dynamic effects is calculation of the spectrum in the absence of exchange. It is easy to see that in the case of cyclohexane such calculation is impracticable, since we need to analyse very complicated n.m.r. spectra (the p.m.r. spectrum of cyclohexane under these conditions can be described as an A_6B_6 system with magnetic nonequivalence).

These difficulties can be avoided to a certain extent by the use of deuteriated compounds[33,34,38]. Isotope effects due to the introduction of heavy hydrogen are assumed to be small and to have no significant effect on the barrier to inversion of the ring. Bovey et al.[33] investigated the proton spectra of undecadeuterocyclohexane. Since $J_{HH}/J_{HD} = \gamma_H/\gamma_D \simeq 7$, the width of the multiplet in the p.m.r. spectra of strongly deuteriated compounds should decrease significantly. Further narrowing of this signal is achieved by the use of $^1H-\{^2D\}$ heteronuclear double resonance. In this case observation of the proton signals at the ^1H frequency (60 MHz) is accompanied by exposure to a second frequency (9.2 MHz), corresponding to ^2D resonance in the same external magnetic field. Use of this technique enabled quite narrow lines (Fig. 3), corresponding to the equatorial and axial positions, to be obtained at low temperatures[34].

The spectra in Fig. 3 already permit approximate methods to be used to calculate rate constants. These methods, based on Eqns. (10) and (11), are often termed *parameter analysis* (Table 2). Many uncertainties generally arise from the use of approximate methods, so that the accuracy of the determination of activation parameters is no better than 10%. Among such uncertainties are the effect of the instrument line width, the temperature dependence of relaxation times and chemical shifts, and the presence of weak spin–spin interactions leading to broadening of the signal. More detailed information on the procedure for correcting for these factors can be found in several published sources[26,27,34,35,40,41].

In some cases it is advisable to simplify the d.n.m.r. spectra by the "fluorine label" method[36] together with the use of deuteriated compounds. The basis of this method is that fluorinated model compounds usually give ^{19}F spectra which are simpler than the proton spectra of the corresponding initial compounds. In particular Roberts[36] suggested that the inversion of cyclohexane (I) should be simulated by that of 1,1-difluorocyclohexane. At +35°C the ^{19}F n.m.r. spectrum of this compound consists of one multiplet (a quintet) due to spin coupling with neighbouring protons. On cooling to −40° the signal broadens, and at −110°C a spectrum of type AB appears, corresponding to two ^{19}F nuclei in a stereochemically rigid structure. The signals of one nucleus are further split into triplets as a result of spin coupling with a pair of neighbouring protons.

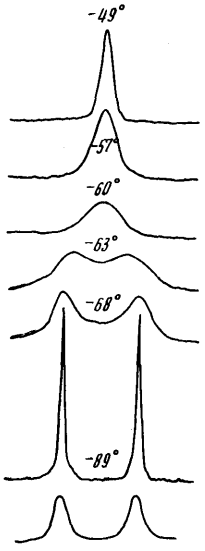


Figure 3. Proton magnetic resonance spectra of C_6HD_{11} with uncoupling from deuterons[34]; the bottom spectrum has been recorded at low temperatures without such uncoupling.

In the temperature range between −100° and +40°C quite complicated changes are observed in the ^{19}F spectrum, owing to mixing of A and B states both as a result of exchange and because of strong coupling between the spins[41]. Nevertheless, the fluorine-19 spectra permit quite accurate analysis of activation parameters by $^{19}F-\{^1H\}$ double resonance.

Dynamic processes can be investigated also by means of non-stationary n.m.r. techniques[35,37,40], for which purpose spectra can be recorded under conditions of rapid flow or pulse methods can be used[42]. Information on rate constants can also be obtained from measurements of relaxation times T_1 (or T_2). In the Carr–Purcell method[37,42], which is most convenient for measuring times T_2, the magnetisation vector M is first subjected to a 90° pulse, i.e. a pulse which turns the vector through 90° and brings it into the xy plane. This is followed by

a series of 180° pulses at intervals of time t_p, $3t_p$, $5t_p$, etc.; as a result of the action of each such pulse the "warmed up" magnetisation vector begins to "run down" and will give spin echo signals at times $2t_p$, $4t_p$, $6t_p$, etc.

Table 2. Approximate methods of calculating rate constants in d.n.m.r. spectroscopy.

Type of method	Basic information	Ref.
Approximation of slow exchange	line width of components $\Delta\nu_{1/2}$ and distance between them $\Delta\nu$ used	7, 18, 34
Approximation of rapid exchange	line width of signal after merging $\Delta\nu_{1/2}$ used	7, 20, 34
Temperature of collapse T_c	temp. determined at which signals merge	7, 34
Temperature of stereochemical rigidity T_r	temp. determined at which appreciable broadening of lines observed at stage of slow exchange	7.39

Because of the occurrence of transverse relaxation processes with time T_2, however, a successive weakening of these signals is observed, which enables T_2 to be measured. If we choose $t_p \ll \tau$, the system will be perceived as static, and damping will correspond solely to dipole–dipole relaxation. If, however, $t_p > \tau$, damping will include a contribution by the exchange process. Equation (10) shows that the contribution by the dynamic process will shorten the effective relaxation time.

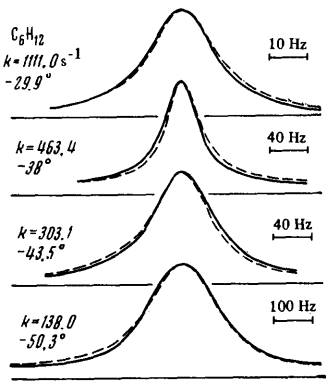


Figure 4. Line-shape analysis in p.m.r. spectra of cyclohexane (100 MHz) at various temperatures[21]: full curves obtained experimentally; broken curves theoretically.

The spin echo method is convenient for investigating rapid dynamic processes. It has been used in particular to measure the time T_2 in cyclohexane (C_6HD_{11}) in the high-temperature range (up to 312°K)[35,37], where continuous n.m.r. methods are ineffective.

It is interesting that spin–spin multiplicity in the region of high-temperature narrowing can be allowed for classically in terms of the Bloch equations[8], which enables methods of *complete line shape analysis* to be applied on the basis of an equation of type (7)§. Calculations by this method are made on an electronic computer[45–48], and sometimes include a stage in which experimental and theoretical spectra are matched by means of special iterative procedures[26,27,49]. The method has been applied to cyclohexane by Inglefield et al.[35] Fig. 4 shows the theoretical spectra having the smallest standard deviation from the corresponding experimental spectra for cyclohexane C_6H_{12}. Satisfactory agreement between the line shapes is evident. Such comparison enables a derived parameter—the rate constant k—to be correlated with an experimental parameter—the temperature.

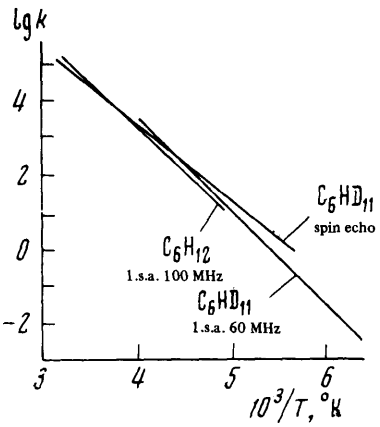


Figure 5. Comparison of various results for the dependence of $\lg k$ on $1/T$ for cyclohexane[35].

Fig. 5 illustrates the variation in $\lg k$ (the rate constant of the inversion of cyclohexane) for three different methods—(a) spin echo[37] and complete line shape analysis at (b) 100 MHz (Fig. 4)[35] and (c) 60 MHz [34] for C_6HD_{11}.

Table 3. Activation parameters for the inversion of cyclohexane and related compounds*.

Compound	Method	Temp. range, °C	E_a, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.	$\Delta G^{\neq}$, kcal mole^{-1}	Ref.
C_6H_{12}	l.s.a., 100 MHz	223—263	10.8±0.2	—3.6	10.8	35
C_6HD_4	spin echo	178—312	9.5	—5.8	10.6	37
$C_6D_{11}H$	l.s.a., 60 MHz	156—256	11.24	+2.8	9.8	35
$C_6D_{11}H$	p.a., 60 MHz	198—226	10.9±0.5	+1.4	10.0	12, 33
$C_6H_{10}F_2$	l.s.a., 56 MHz	200—320	9.5	—3.3	0.0	41
C_6H_{12}	p.a., 60 MHz	168—218	12.0	+4.9	9.9	32

* l.s.a. = line-shape analysis; p.a. = parameter analysis.

The results of the various investigations of the inversion of cyclohexane (Table 3) enable certain comments to be made on the accuracy of the measurements of activation parameters. Interest in this question has arisen from

§ Dynamic n.m.r. spectra under conditions of multiposition exchange have been considered in Refs. 43 and 44.

the fact that, despite the wide application of d.n.m.r. spectroscopy in various kinetic investigations, the accuracy of the measurement of activation parameters is small. As a consequence, the analysis of dynamic effects is restricted in many cases to a qualitative picture (establishment of the actual fact of exchange, determination of the approximate temperature range, estimation of the free energy of activation). Recent detailed analyses of the errors involved in the use of various forms of d.n.m.r. [21,26,27,35,39,40,49] lead to certain conclusions.

Approximate methods of analysis (Table 2) yield activation parameters with an accuracy of at best 10%. In principle an accuracy of 2–3% can be achieved by line shape analysis, provided that several conditions are observed, primarily careful experimental recording of the spectra. Important factors are slow passage, absence of phase distortions and amplitude non-linearities, control of resolution throughout the temperature range, and accurate measurement of temperature [39]. Experimental data can be compared only if conditions (solvent, concentration) are fully adequate [11,26]. On the other hand, methods of line shape analysis should be adequate in allowing for relaxation, the temperature dependence of the resonance frequencies, and the character of the iteration procedures [27,49].

In the analysis of complicated spectral systems (e.g. cyclohexane) it is possible to use simpler model systems. It must always be borne in mind that the model may not be adequate to the system. In particular, when strongly deuteriated models are used (C_6HD_{11} in the case of cyclohexane), the total secondary isotope effect may exceed the error of measurement [4]. Fluorinated models (systems with a fluorine label), while being attractive experimentally, must be all the more inadequate models.

Investigations of the activation parameters for inversion in cyclohexane show that the possibility of making measurements over a wide temperature range is an important factor.

It is interesting that, in spite of the poor accuracy with which the activation functions E_a and $\Delta S^{\neq}$ are determined (especially by approximate methods), the free energy of activation can be determined very accurately [10,11,39,49] (Table 3). The reason is that the value of $\Delta G_T^{\neq}$ is obtained directly from data on rate constants (Eqn. 1), whereas E_a is evaluated as the difference between two sometimes closely similar values of $\lg k$ (Eqn. 4). Kessler [10] gave a curious graph for the activation functions of rotation in dimethylformamide: a plot of E_a against $\Delta S^{\neq}$ showed that values of E_a obtained experimentally in various studies cover a range of 8–28 kcal mole^{-1}. [1] However this variation is almost linear, so that values of $\Delta G_T^{\neq}$ differ by at most ±1 with a mean value of 21.5 kcal mole^{-1}.

Summarising, we can say that d.n.m.r. spectroscopy at present has diverse ways of recording spectra and techniques for analysing the data, which permits both the rapid and straightforward estimation of free energy of activation and also the accurate determination of activation parameters.

IV. CLASSIFICATION ACCORDING TO TYPE OF SPECTRA OF THE EXCHANGEABLE SPIN SYSTEMS

Where spin multiplicity is present the d.n.m.r. spectra can be classified in conformity with the type of n.m.r. spectra (according to Pople's nomenclature [12,13,23] characteristic of the separate instantaneous structures.

1. The ^{19}F spectrum of 1,1-difluorocyclohexane, under conditions of uncoupling from the protons [41] at sufficiently low temperatures, is of type AX, where A is a ^{19}F nucleus in an axial position, and X a ^{19}F nucleus in an equatorial position, which can be denoted as the A(1)X(2) type. As a result of inversion of the ring the fluorine atoms exchange positions. Thus the whole spectrum under conditions of exchange is described by the relation

$$\begin{array}{c} A(1)\,X(2) \rightleftarrows X(1)\,A(2), \\ \text{or}\quad AX \rightleftarrows XA\ . \end{array} \qquad (12)$$

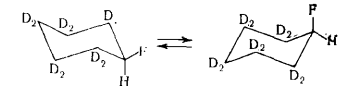
In principle this case of exchange is described more rigorously by the equation

$$AB \rightleftarrows BA \qquad (13)$$

which takes into account the mixing of the eigenfunctions of nuclei A and B due to strong spin coupling. In the limit of rapid exchange (i.e. as $\tau \to 0$) the spectrum is a singlet in both cases (12) and (13). In systems with strong mixing of the spin functions of the nuclei the lifetime of a state at the instant of collapse of the signals in the spectrum can be estimated [50] by means of the formula

$$\tau_c = \frac{2}{\pi}[(\nu_A - \nu_B)^2 + 6J^2]^{-1/2}\ . \qquad (14)$$

2. In contrast to the exchange described by Eqns. (12) and (13), corresponding to so called interchange [11,31], cases are theoretically possible in which the individual structures are not identical. Let us examine in particular the d.n.m.r. spectra of decadeuterofluorocyclohexane (II) under conditions of conformational mobility [51]



$$\text{or}\quad F_{eq}\,H_{ax} \underset{k_1}{\rightleftarrows} F_{ax}\,H_{eq}$$

$$A_1X_1 \underset{k_2}{\rightleftarrows} A_2X_2\ . \qquad (15)$$

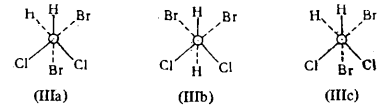
The different subscripts for AX systems in this case show that the spectral parameters of the systems are different. Processes of type (15) are in general non-degenerate ($k_1 \neq k_2$). In the case of rapid exchange the spectrum corresponds to a system of type AX with the average parameters

$$\begin{aligned} \langle\delta_A\rangle &= p_1\delta_{A_1} + p_2\delta_{A_2}\ , \\ \langle\delta_X\rangle &= p_1\delta_{X_1} + p_2\delta_{X_2}\ , \\ \langle J_{AX}\rangle &= p_1J_{A_1X_1} + p_2J_{A_2X_2}\ , \end{aligned} \qquad (16)$$

where

$$p_1 = \frac{k_2}{k_1+k_2};\quad p_2 = \frac{k_1}{k_1+k_2}\ .$$

3. A system of two nuclei with slightly non-equivalent instantaneous structures is illustrated by 1,1,2,2-tetrasubstituted ethanes, e.g. HCl_2C-CBr_2H. [51] Rapid rotation about the carbon–carbon bond usually occurs in these molecules, which is clearly depicted by Newman projections as the three structures



(IIIa) (IIIb) (IIIc)

Two of them (a and c) are gauche (or skew) forms, and one a *trans*-form. In the absence of exchange the spectra of structures (IIIa), (IIIb), and (IIIc) are of types A*B*, A**B**, and A*B* respectively, where it is implied that the gauche isomers are spectrally indistinguishable.

Rotation about the carbon–carbon bond is described by the equations

$$A^*B^* \underset{k_2}{\overset{k_1}{\rightleftarrows}} A^{**}B^{**} \underset{k_1}{\overset{k_2}{\rightleftarrows}} A^*B^* \qquad (17)$$

where in general $k_1 \neq k_2$, since the statistical weights of forms (a) and (b) may differ.

A more complicated situation was examined by Newmark and Sederholm [52,53] for the case of completely non-degenerate exchange (rotation about the carbon–carbon bond in fluorinated ethanes)

$$A_1B_1 \rightleftarrows A_2B_2 \rightleftarrows A_3B_3 . \qquad (18)$$

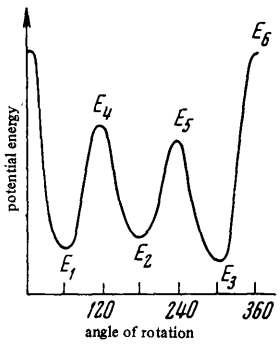


Figure 6. Form of the potential-energy surface for rotation about carbon–carbon bond in unsymmetrically fluorinated ethanes.

The potential-energy curve for such a process is characterised by three maxima E_4, E_5, E_6 and three minima E_1, E_2, E_3 corresponding to three stable rotamers (Fig. 6). Analysis of the stereochemically rigid case will give the populations of the states, i.e. the values of E_1, E_2, and E_3. Determination of the activation barriers E_4, E_5, and E_6 involves analysis of the complete kinetic scheme [52].

4. The most complicated type of system comprising three nuclei with interchange [30] involves exchange among six possible states—ABC, ACB, BAC, CBA, BCA, and CAB—in particular the cyclic exchange

$$ABC \rightleftarrows BCA \rightleftarrows CAB \qquad (19)$$

or exchange between two positions

$$ABC \underset{k_{21}}{\overset{k_{12}}{\rightleftarrows}} BAC . \qquad (20)$$

The latter type of exchange process can be illustrated by the spectra calculated by Binsch [30] (Fig. 7). With very slow exchange the spectrum is described by the parameters (all in Hz) $\nu_A = 19.6$, $\nu_B = 22.9$, $\nu_C = 52.7$, $J_{AB} = 12.3$, $J_{BC} = 7.3$, and $J_{AC} = -17.7$. The spectrum is quite complex, and combination transitions are observed. Increase in the rate k is accompanied by complicated changes in the spectrum, not susceptible to simple analysis. When sufficiently high rates are reached the system passes into an effective A_2B type (the spectrum at k = 10 000 s^{-1} in Fig. 7). Results of an analysis of d.n.m.r. spectra have been published for complete interchange in a system of three spins [31].

5. A system of four spins is represented by the spectrum of formamide $H_2{}^{15}NCHO$, [54] described in general as an ABCX system (where X is the ^{15}N nucleus and C the formyl proton). Here rotation about the partly double carbon–nitrogen bond leads to an exchange process of the type

$$ABCX \rightleftarrows BACX . \qquad (21)$$

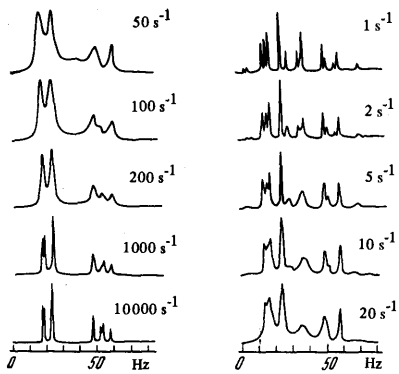


Figure 7. Theoretical spectra [30] calculated for various rate constants by means of a d.n.m.r. programme for exchange of the type ABC ⇌ BAC.

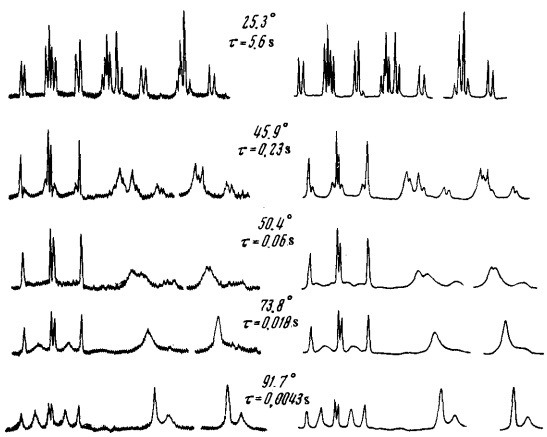


Figure 8. Experimental (on left) and theoretical spectra in formamide $H_2{}^{15}NCOH$ (exchange of type ABCX ⇌ BACX) at various temperatures and rate constants [54].

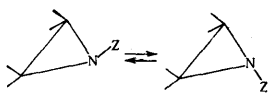
Experimental investigations of this spectrum made at various temperatures by Drakenberg and Forsen [54] are illustrated in Fig. 8. Rate constants were calculated by line shape analysis. A necessary first stage in the calculation was to analyse the ABCX spectrum in the absence of exchange. This gave values of chemical shifts and bond constants (δ_H, J_{HH}, J_{NH}), which were then used in calculating the spectra during exchange by means of a DENSMAT programme [54,55]. A theoretical spectrum characterised by a definite value of k was then selected

by comparison with the experimental spectrum (Fig. 8), after which the activation parameters were calculated (Table 4). This rigorous approach permitted a significant improvement in the accuracy of determination of the activation parameters in comparison with previously published values.

Table 4. Activation parameters in formamide.

Solvent	E_a, kcal mole^{-1}	lg$A$	$\Delta H^{\neq}$, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.	$\Delta G^{\neq}_{300°}$, kcal mole^{-1}	Ref.
Pentan-2-one	19.2±0.2	13.2	18.2±0.2	2.7±0.6	17.55±0.2	54
Acetone	13±8	—	—	—	—	55

Another example is provided by inversion in substituted aziridines[57,58]



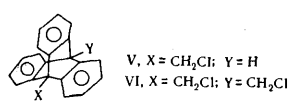
(IVa) (IVb)

The p.m.r. spectrum of the four protons in this compound is described as the AA'BB' system. As a result of rapid inversion at the nitrogen atom, represented by the equation

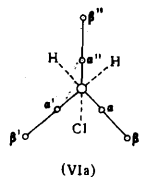
$$AA'BB' \rightleftarrows BB'AA', \qquad (22)$$

the spectrum is converted into a singlet.

6. Rather complicated spin systems have been examined theoretically by Binsch and Kleier[31] (including $A_3B_3 \rightleftharpoons C_3D_3$, $A_3B_3 \rightleftharpoons B_3A_3$, and $AA'BB' \rightleftharpoons CC'DD'$) using symmetry properties. These systems correspond to the upper limit of the possibilities of the best modern electronic computers[30,31]. The investigation of dynamic effects in complicated spin systems is therefore usually based on a series of simplifying assumptions. A very instructive example is the study of hindered rotation about $C_{(9)}$–CH_2Cl bonds in chloromethyltriptycenes[59] substituted at positions 9 and 10 (V, VI)



V, X = CH_2Cl; Y = H
VI, X = CH_2Cl; Y = CH_2Cl



(VIa)

The spectrum of the initial compound (triptycene) consists of two groups of signals with their centres at 5.50 (bridge protons) and at 7.50 and 7.00 ppm (aromatic protons). The spectrum of the latter is quite simple and of type AA'BB' owing to the high symmetry ($C_{(9)}$–$C_{(10)}$ is a threefold symmetry axis). Replacement of the 9- and 10-protons by chloromethyl groups produces significant changes in the spectrum: both parts become notably broader (part A to a greater extent) in the spectrum measured at room temperature. The symmetry of the system may be assumed to be diminished by the hindered rotation of the chloromethyl group; the individual structure is shown as a Newman projection (VIa). On heating, the spectrum becomes narrower, and passes into type AA'BB' at 100°C (Fig. 9). Estimates of the barrier to rotation in this system yielded the value $\Delta G^{\neq}_{300°} = 16$ kcal mole^{-1}.

Similar changes are observed with the monosubstituted 9-chloromethyltriptycene[60], where rapid rotation transforms an extremely complicated superposition of ABCD spectra characteristic of each ring into a comparatively simple spectrum of ABCD type. In this latter case the exchange process is degenerate, and can be represented by a scheme involving all twelve [aromatic] protons in the molecule:

$$A_1B_1C_1D_1A_2B_2C_2D_2A_1B_1C_1D_1 \rightleftarrows A_1B_1C_1D_1A_1B_1C_1D_1A_2B_2C_2D_2 \rightleftarrows \rightleftarrows A_2B_2C_2D_2A_1B_1C_1D_1A_1B_1C_1D_1 . \qquad (23)$$

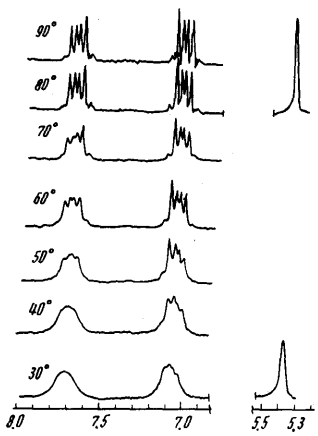
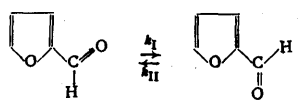


Figure 9. Proton magnetic resonance spectra of 9,10-bischloromethyltriptycene at various temperatures[59].

The exchange scheme for the disubstituted compound will be still more complicated owing to interaction of the chloromethyl groups lowering the symmetry of the system. It is significant that in these examples the spectra are almost incapable of analysis under conditions of stereochemical rigidity.

V. COMBINATION WITH OTHER METHODS OF INVESTIGATION OF THE KINETICS OF CHEMICAL REACTIONS

In several cases the accuracy of the measurement of activation parameters can be significantly improved by combining d.n.m.r. with other methods of determining rate constants[15]. An instructive example is provided by hindered rotation in 2-furaldehyde



(VIIa) (VIIb)

In the p.m.r. spectrum of this compound at room temperature the aldehydic proton is observed as a doublet of doublets with constants $J_{CHO(H_{(4)})}$ and $J_{CHO(H_{(3)})}$ of 0.3 and 0.77 Hz. When the temperature is lowered to −115°C two signals are observed in the region of aldehydic protons, the intensity ratio being 1 : 10. These signals are doublets with separations of 0.85 and 1.10 Hz (low- and high-field signals). The chemical shifts showed that the

isomer (VIIa) is present in higher concentration: i.e. $k_{II} > k_I$ and $\delta G = \Delta G_I^{\neq} - \Delta G_2^{\neq} > 0$. The activation parameters for processes k_I and k_{II} were calculated from the temperature-dependent p.m.r. spectra by means of McConnell's modification of Bloch's equation for unequal p_A and p_B.[61]

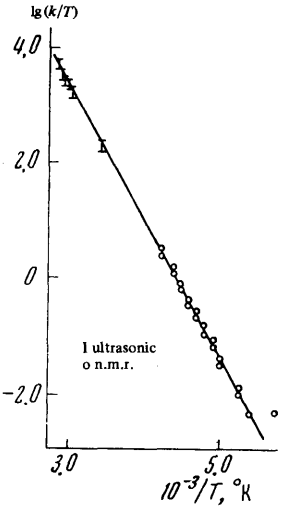
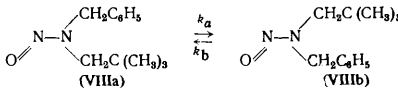


Figure 10. Dependence of lg (k/T) on $1/T$ for rotation in 2-furaldehyde from n.m.r. and ultrasonic relaxation data[62].

The same system has since been investigated by means of ultrasonic relaxation[15], which permits study of equilibria established with rates of 10^5–10^6 s^{-1}. Fig. 10 illustrates the dependence of $\lg k_A/T$ on $1/T$ based on the combined results of n.m.r. and ultrasonic relaxation[62]. Use of an extended temperature range (from −100° to +90°C) enables extremely reliable values to be obtained: E_a = 11.5 ± 0.5 kcal mole^{-1} and the frequency factor $A = 2 \times 10^{13}$ s^{-1}.

In many cases d.n.m.r. can be combined with "visual" kinetic methods (Table 1). Only the isotopic labelling version of these methods is applicable to degenerate exchange processes[1]. The usual methods for measuring concentrations of states (including n.m.r. with integration of the signals) can be applied to non-degenerate exchange processes. We shall examine an investigation of a dynamic process using both n.m.r. methods (in the corresponding temperature range, of course).

Jaeschke et al.[63] have examined equilibrium and exchange in benzylneopentylnitrosamine and detected rotation about the partly double bond:



In the temperature range 0–50°C the rates of both processes are small ($< 10^{-4}$ s^{-1}), so that the slow establishment of equilibrium in the system can be investigated by integration in the n.m.r. spectra, for which purpose a pure rotamer is isolated and appearance of the second rotamer is observed. Above +100°C a gradual broadening of the signals in the nitrosamine spectrum is observed, which enables d.n.m.r. spectroscopy to be used in this range.

These workers[63] concluded from a complete survey of various methods for calculating rate constants from n.m.r. spectra that closely similar results are obtained by parameter analysis and by line shape analysis. In view of the diversity of initial line shapes and the uncertainties in the procedure for matching experimental and theoretical spectral curves, parameter-analysis methods (line widths, distance between signals) were mostly used.

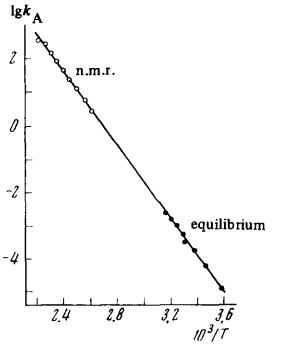


Figure 11. Dependence of $\lg k$ on $1/T$ for the isomerisation of benzylneopentylnitrosamine[63].

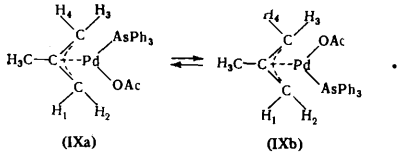
Fig. 11 illustrates the dependence of $\lg k_a$ on $1/T$ based on both equilibrium (integration at low temperatures) and d.n.m.r. (at high temperatures) data. The linearity of this relation enables the two methods to be compared (Table 5), with the following significant conclusions: (*a*) the accuracy of the determination of activation energy from d.n.m.r. spectra is ±10%; (*b*) this is substantially inferior to the accuracy obtained by the equilibrium method (±1.5%); (*c*) use of data from both methods yields an improvement to 0.5%; and (*d*) in all cases the determination of $\Delta G^{\neq}$ is more accurate than that of E_a.

Table 5. Comparison of activation parameters for the process (VIIIa) → (VIIIb) in benzylneopentylnitrosamine obtained by equilibrium method and from n.m.r. spectra[63].

Method	E_a, kcal mole^{-1}	lg A	$\Delta G^{\neq}$, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.	Temp., range, °C
Dynamic n.m.r.	25.3±2.2	14.8±1.2	22.0	+6.7	112—182
Equilibrium (integration)	24.2±0.3	14.1±0.2	22.1	+3.5	0—50
Mean	24.7±0.1	14.5±0.1	22.0	+5.2	0—182

Furthermore, the temperature range of the measurement of rate constants can be extended by applying various modifications of d.n.m.r. Mention has already been made

of spin echo methods, useful in the investigation of rapid dynamic processes. Double magnetic resonance (saturation transfer effect) has recently been used to investigate exchange processes where rates of exchange are not too high[64]. An example is the study of pseudorotation in a π-allylpalladium complex[65], sometimes termed *π-rotation*[65]



(IXa) (IXb)

As a consequence of such rotation the spectrum, originally consisting of individual signals $H_1H_2H_3H_4$ somewhat broadened by spin–spin interactions, is averaged out on heating, with the proton H_1 exchanging with H_4, and the proton H_2 with H_3. The occurrence of exchange in the slow stages was proved in this case by the use of double resonance methods, the most detailed description of which has been given by Hoffman and Forsen[64] in a survey of various applications of double resonance.

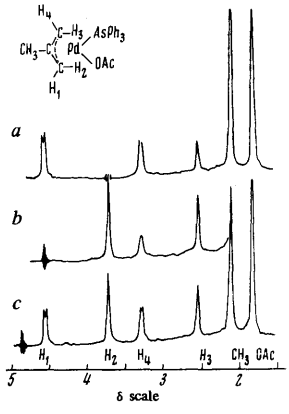


Figure 12. Proton magnetic resonance spectra of π-allylpalladium complex: a) single resonance; b) exposure of signal of proton H_1; c) exposure of signal of proton H_2.[65]

If we imagine a system in which a nucleus can occupy positions A and X, application of the Bloch–McConnell equations gives for the longitudinal magnetisation of nucleus A the formula

$$\frac{dM_z}{dt} = \frac{M_0^A - M_z^A}{T_{1A}} - \frac{M_z^A}{\tau_A} + \frac{M_z^B}{\tau_B} \qquad (24)$$

where M_0 is the equilibrium magnetisation and τ_A the lifetime of state A. If the signal of nucleus B is saturated by means of a second high-frequency field (i.e. $M_z^B \to 0$), we obtain

$$\frac{dM_z}{dt} = \frac{M_0^A}{T_{1A}} - \frac{M_z^A}{\tau_{1A}} \qquad (25)$$

where

$$\frac{1}{T_{1A}} = \frac{1}{\tau_A} + \frac{1}{T_{1A_0}} \quad .$$

The solution of this equation for the equilibrium case is given by

$$M_z^A(t \to \infty) = M_0^A \frac{\tau_{1A}}{T_{1A}} \quad . \qquad (26)$$

Thus the magnetisation in state A falls with increase in the rate of exchange ($\tau/T_{1A} \to 0$). This has been termed the saturation transfer effect. If the signal of the proton H_1 is now exposed to the second high-frequency field, the signal intensity of the proton H_4, bound to H_1 by exchange, becomes weaker. Similarly, exposure of the signal of proton H_2 produces a fall in signal intensity of the proton H_3 (Fig. 12). Thus proof of the occurrence of a dynamic process has not required the measurement of a temperature dependence.

Equation (26) can in principle be used to measure the lifetime τ (from the relative fall in intensity of the signal of state A). However, such measurements encounter certain difficulties (incomplete saturation of signal of state B, allowing for the relaxation time T_{1A}). Use of the saturation transfer effect makes it possible in principle to measure slower processes than in the case of single resonance, since as a rule $T_1 > T_2$, so that the effect can be expected to be appreciable at earlier stages of exchange than can the line-broadening effect (τ/T_2).

The temperature range over which rate constants can be measured can be extended also by the use of carbon magnetic resonance (c.m.r.) spectroscopy. Such spectra are usually recorded under conditions of uncoupling from protons, with a consequent significant improvement in the signal/noise ratio both as a result of collapse of the multiplet structure and because of the Overhauser effect. This is responsible for the first advantage of c.m.r. over p.m.r. spectroscopy, since there is no need to correct for the multiplet character of the spectra. Furthermore, the range of chemical shifts of carbon nuclei is about thirty-fold the range for protons. Equation (11) shows that, for the line width in the case of rapid exchange, it becomes possible to measure faster processes. We have in fact, for rate constants measured at the upper limit of rapid exchange, the ratio

$$k_C/k_H = (\Delta\nu_C)^2/(\Delta\nu_H)^2 \simeq (30)^2\gamma_C^2/\gamma_H^2 \simeq 45$$

where $\Delta\nu_C$ and $\Delta\nu_H$ (Hz) are the ranges of chemical shifts for ^{13}C and ^{1}H spectra respectively. This usually enables rate constants to be measured from c.m.r. spectra at temperatures 50–60 deg higher than in the case of p.m.r. spectra. An example of the use of carbon magnetic resonance for this purpose will be given in Section VI.

VI. FLUCTUATING OR STEREOCHEMICALLY NON-RIGID SYSTEMS

Two main groups—intermolecular and intramolecular processes—can easily be distinguished from the range of dynamic phenomena studied by d.n.m.r. spectroscopy. Intermolecular processes are not discussed in the present Review: references are merely given to sufficiently comprehensive and competent reviews on general[7,8] and special aspects (proton exchange in alcohols, acids, etc.[66], dissociation–recombination processes in organometallic compounds[67]). Several examples of intramolecular processes have been given in Sections III–V. A number of up-to-date reviews have been published on rotations about various types of partly double or sterically hindered bonds[10] and on inversions of various cyclic organic molecules[68].

Recent years have seen a widening use of d.n.m.r. spectroscopy for the investigation of various rearrangements, i.e. processes in which, in contrast to rotations and inversions, some bonds are broken and new bonds are formed. Degenerate intramolecular rearrangements, during which the molecule passes "into itself", are of especial theoretical interest. The individual structures formed during such rearrangements are termed instantaneous structures. In contrast to the classical method of examining rearrangements—isotopic labelling—d.n.m.r. spectroscopy involves considerably fewer technical difficulties and also enables rapid processes to be examined (Table 1). Examples of degenerate rearrangements are extraordinarily varied and are encountered in organic [69], inorganic [70], and organometallic [71] systems. Several terms have been suggested to denote systems capable of degenerate processes—stereochemically non-rigid systems (Muettertis [70]), fluctuating molecules (Doering and Roth [69], Cotton [71]).

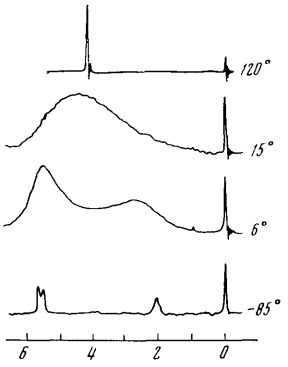
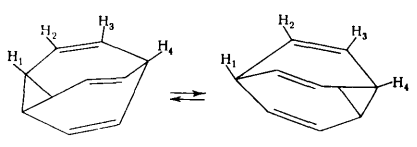


Figure 13. Proton magnetic resonance spectrum of bullvalene measured at various temperatures.

Perhaps the most impressive fluctuating molecule is that of bullvalene, whose existence was predicted by Doering and Roth [69]. The compound itself was prepared and described by Schröder [72]. At sufficiently low temperatures its spectrum consists of two poorly resolved multiplets (Fig. 13): the signal at 5.65 ppm corresponds to the six olefinic protons, and that at 2.08 ppm to the remaining four protons. It is interesting that the proton attached to the tertiary carbon atom gives resonance in the same region as those of the three-membered ring, probably as a result of the magnetically anisotropic effect of this ring. Broadening of both groups of signals is detected on heating above 0°C, the change occurring more rapidly in the high-field signal. On further heating (to 100°C) a singlet appears for all the protons (Fig. 13) with a shift of 4.42 ppm.

Exchange involving all positions is obviously occurring in this system. One step in such exchange is



in which the proton H_1 "rearranges" into H_4, proton H_3 into H_2, proton H_4 into H_1, and H_2 into H_3. At the next stage in the rearrangement the olefinic protons H_2 and H_3 may change positions with those attached to the extreme carbon atoms, and so on. The multiplicity of paths in such a dynamic process and of individual instantaneous structures (computed [69] as 1 209 600) led Doering [69] to introduce the term "fluctuating" molecules. Saunders and Hagen [46] used a programme for multipositional exchange to calculate the activation energy of degenerate rearrangement in bullvalene as $E_a = 11.8$ kcal mole^{-1}, while the entropy of activation is close to zero.

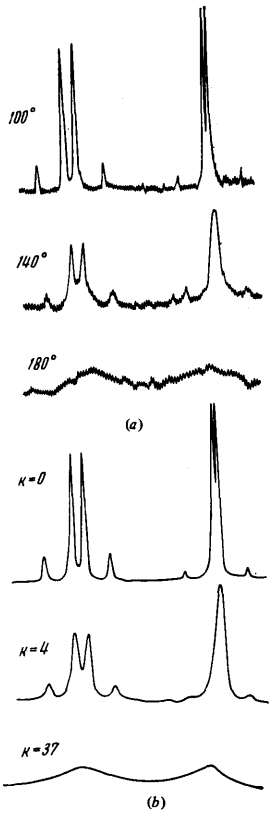
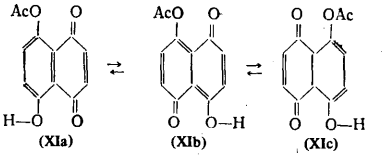


Figure 14. Experimental (a) and theoretical (b) p.m.r. spectra of monoacetatonaphthazarin at various temperatures [73].

An interesting rearrangement has been discovered by Calder et al. [73] in an investigation of the temperature-dependent spectra of acetatonaphthazarin (XI)

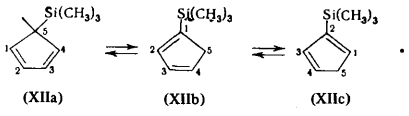


The p.m.r. (100 MHz) spectrum of this compound measured at 100°C (Fig. 14) exhibits two groups of signals

giving spectra of type AB—at 6.70 and 6.67 ppm with a constant J_{HH} = 10 Hz, and at 7.20 and 7.10 ppm with J_{HH} = 8.1 Hz—from which the high-field signals can be assigned to protons of the quinonoid ring. On heating above 140°C the signals begin to broaden, which indicates the occurrence of a dynamic process on the pattern $A_1 \rightleftharpoons A_2$, $B_1 \rightleftharpoons B_2$. The dynamic process may be assumed to involve formation of the product (XIb), which is intermediate (but not transitional) and corresponds to a "jump" by the proton in the hydrogen bond. However, the p.m.r. spectra do not reveal the presence of (XIb), and hence the acetyl rearrangement and the proton shift take place synchronously.

In order to estimate the parameters of the rearrangement theoretical spectra were calculated by the use of a d.n.m.r. programme. The free energy of activation of this process proved to be 22.5 kcal mole^{-1}. Conditions of rapid exchange could not be attained even at 180°C, but available data suggest that the acetyl exchange occurs intramolecularly. It may be supposed that a single spectrum of type AB should be observed at high temperatures.

An example of a fluctuating organometallic molecule is the cyclopentadienylsilicon compound $C_5H_5Si(CH_3)_3$.[39,74] As a consequence of prototropic rearrangement—characteristic also of cyclopentadiene itself[75] and of its alkyl derivatives[76]—this compound may be present in one of the forms (XII):



(XIIa) (XIIb) (XIIc)

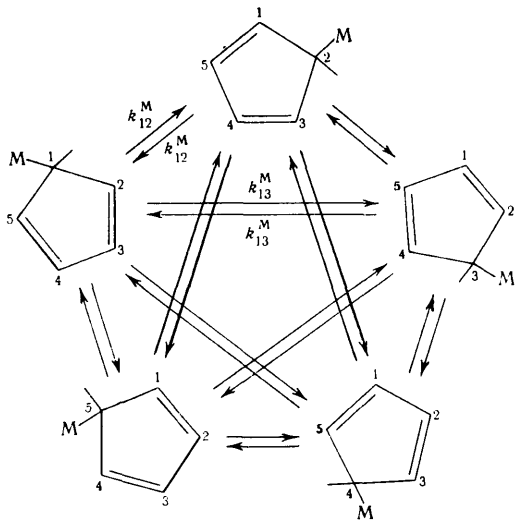


Figure 15. Scheme of degenerate metallotropic rearrangement in cyclopentadienyl derivatives of metals C_5H_5M.

This process is non-degenerate, and is characterised in general by complicated kinetic and equilibrium parameters. Up to temperatures of 100°C, however, the rate constants of prototropic rearrangement are small, so that the process remains slow on the n.m.r. time scale.

The p.m.r. spectrum at room temperature exhibits signals from all three isomers (XII) (a solution of the compound in benzene gives three signals due to the methyl groups with the intensity ratio A : B : C = 90 : 9 : 1). Integral measurements indicate that equilibrium in the compound is displaced towards the isomer (XIIa). Furthermore, a second dynamic process—metallotropic rearrangement, shown diagrammatically in Fig. 15—has been noted with this isomer. The p.m.r. spectrum at −20°C and below includes the AA'BB'X type (Fig. 16) corresponding to the isomer (XIIa), where X is a methine proton (at 3.00 ppm). The following stages of the dynamic process are observed on heating—broadening of the multiplet structure, coalescence of the signals in the AA'BB' part, collapse of all signals, and the appearance of one signal (a singlet) at 5.87 ppm¶.

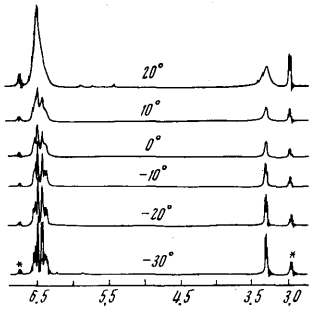
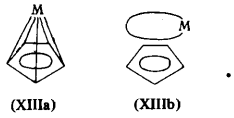


Figure 16. Proton magnetic resonance spectra (100 MHz) of $C_5H_5Si(CH_3)_3$ at various temperatures[39]. Signals marked with an asterisk (*) correspond to contamination with vinyl isomers.

Slow migration of the heavier metals (tin, mercury, gold) in cyclopentadienyl compounds can be achieved only at very low temperatures (around −150°C), and it becomes difficult to choose between alternative structures—true (XIIIa) and effective (XIIIb) centrosymmetric complex



(XIIIa) (XIIIb)

In such cases ^{13}C n.m.r. is useful (Section V), which can be illustrated by a specific example. Migration of the metal across the ring in cyclopentadienyltrimethylstannane $C_5H_5Sn(CH_3)_3$ has such a low activation energy (~ 6 kcal mole^{-1} [77]) that the line width in the proton spectra remains < 1 Hz right down to around −80°C (the most practicable temperatures when carbon disulphide is used as solvent). In the carbon spectra[78] (Fig. 17) significant broadening is already observed at −45°C.

In certain cases accurate line-shape analysis in the n.m.r. spectrum during exchange enables the mechanism of the process to be determined. In cyclopentadienyl

¶ The latter stages of the dynamic process are not shown in Fig. 16, since at high temperatures cyclopentadienyl compounds of silicon dimerise quite rapidly.

derivatives of metals, in particular, it is theoretically possible to choose one of the mechanisms[79] (Fig. 18)—(*a*) 1,2-migration of the metal, (*b*) 1,3-migration, and migration to any position in the ring equally probable, either via a centrosymmetric transition state (*c*) or by intermolecular exchange (*d*). Until quite recently it was both experimentally and theoretically problematical to separate these mechanisms. Experimental determination of the predominant migration was first achieved by Cotton et al.[79] from the unsymmetrical collapse in the d.n.m.r. spectra. This idea has since been used in many studies[39,48,77,78] of the fluctuating behaviour of the cyclopentadienyls of various metals.

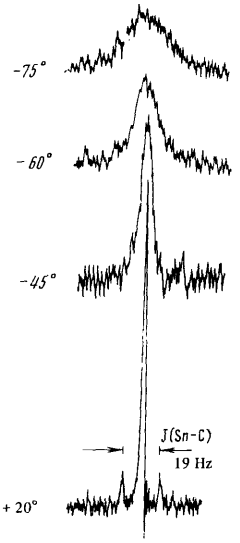


Figure 17. Carbon-13 n.m.r. spectra of trimethylstannylcyclopentadiene at various temperatures[78].

It can be postulated[79,78] that the assignment of the lines in the scheme illustrated by Fig. 15 is such that the low-field signal in the general spectrum AA'BB'X is due to the 1,4-protons of the isomer (XIIa). In a single act of migration the frequencies of the protons will then undergo different changes for the different mechanisms of migration (Table 6). Thus in the case of 1,2-migration the signal A merges with B and X, while signal B merges with A and with the other B (null exchange) (Table 6). The signals of protons A will therefore undergo greater broadening than those of protons B. Thus unsymmetrical broadening of the signals in the olefinic region may be observed at the stage of exchange at which the migration rate constant is comparable with the shift $\Delta\nu_{AB}$ (expressed in frequency units Hz). In the case of the alternative assignment $\delta_A = \delta_{2,3}$ and $\delta_B = \delta_{1,4}$ the signal B will obviously undergo greater broadening.

Examination of the p.m.r. spectra of cyclopentadienyltrimethylsilicon at temperatures near 0°C (Fig. 16) reveals greater broadening of the up-field signal in the AA'BB' part. Unfortunately, *a priori* assignment of the signal in the olefinic part of the spectrum is not possible. Detailed analysis of the spectrum by double resonance under conditions of stereochemical rigidity[39] shows that $\delta_A = \delta_{2,3}$ and $\delta_B = \delta_{1,4}$. Thus silicon undergoes 1,2-migration in its cyclopentadienyl compounds. Correct assignment of the signals is of decisive importance in selecting the predominant mechanism of migration.

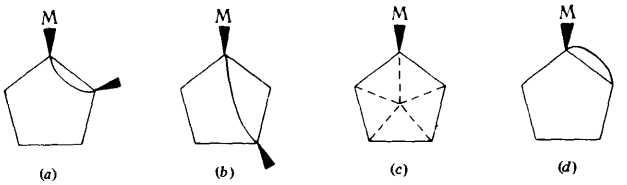


Figure 18. Possible modes of migration of metal in cyclopentadienyl compounds (intramolecular): a) 1,2-displacement; b) 1,3-displacement; c) through a centrosymmetric transition state; d) intermolecular migration.

There is usually no difficulty in eliminating the remaining mechanisms of migration. Unsymmetrical broadening is not observed when migration takes place through a centrosymmetric state or by intermolecular exchange. These two mechanisms can be distinguished by the use of additional data, in particular on the dependence of the rate of migration on the solvent and on the concentration of the solution.

Table 6. Transpositions of nuclei in exchanges involving 1,2- and 1,3-migration.

Position of proton	Position of signals in spectrum ($\delta_A > \delta_B$)		
	initial	final	
		1,2-shift	1,3-shift
5	X	A	B
1	A	B	B
2	B	B	A
3	B	A	X
4	A	X	A

In calculating the activation parameters of metallotropic rearrangement we encounter difficulties that are sufficiently common not to receive special mention. These difficulties arise primarily from the presence of strong spin coupling, which is apparent in the complicated multiplet structure of the signals in the absence of exchange (spectra of type AA'BB'X). Certain technical difficulties connected with the great size of the computations derive from the multipositional character of the exchange (five-position exchange allowing for magnetic non-equivalence—Section IV). In the limit of slow exchange the line width of the methine proton can be used to calculate the rate

constants. On the assumption of a mechanism of 1,2-migration we can write for the line widths of signals A, B, and X[39]

$$\pi\delta\nu_A = \left(\frac{1}{T_2}\right)_A + \frac{1}{\tau}\ ,$$
$$\pi\delta\nu_B = \left(\frac{1}{T_2}\right)_B + \frac{1}{2\tau}\ , \qquad (28)$$
$$\pi\delta\nu_X = \left(\frac{1}{T_2}\right)_X + \frac{1}{\tau}\ .$$

In the region of rapid exchange we can start from the approximations $\delta_A = \delta_B$, $p_A = 4/5$, $p_X = 1/5$. From Eqn. (11) we can obtain

$$k_{eff} \approx \frac{1.61 \cdot (\Delta\nu)^2}{\Delta\nu_{1/2} - (\Delta\nu_{1/2})^0} \qquad (29)$$

where $\Delta\nu$ (in Hz) is the distance between the AB and the X parts of the spectrum, and $\Delta\nu_{\frac{1}{2}}$ is the line width with infinitely rapid exchange.

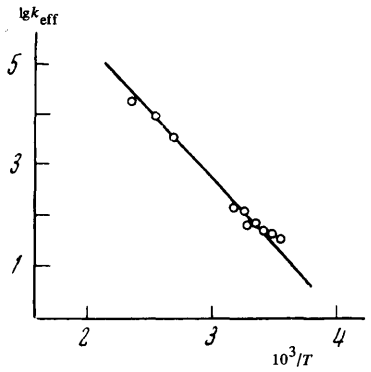
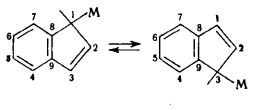


Figure 19. Dependence of lg$k$ on $1/T$ for metallotropic rearrangement in $C_5H_5Si(CH_3)_3$.[39]

Fig. 19 illustrates the dependence of lgk_{eff} on $1/T$ for migration in cyclopentadienyltrimethylsilicon. At low temperatures values of k_{eff} somewhat exceed k_{true}, since initial dipole–dipole relaxation and the multiplet structure make a contribution to the line width. At high temperatures, on the other hand, values of k_{eff} are rather lower than k_{true} owing to neglect of the relaxation term $(1/T_2)$ in Eqn. (28). Extrapolation from each section thus leads to underestimates of the activation energy E_a. A linear approximation to the dependence of lg$k$ on $1/T$ yields for the activation energy E_a and the entropy of activation $\Delta S^{\neq}$ values of 13 kcal mole^{-1} and −9.2 e.u. respectively[39].

Migration of the metal is detected also in indenyl derivatives of Group IVb elements[80,81]:



(XIVa) (XIVb)

The p.m.r. spectra of these compounds show complicated temperature relations, from which it is difficult to calculate rate constants. These difficulties are due primarily to overlapping between the signals from protons of aromatic and five-membered rings. At low temperatures (−30°C with M = $Sn(CH_3)_3$) the spectrum of the protons divides into two parts—ABCD (aromatic protons 4–7) and ABX (protons 3–1). Heating produces a gradual broadening of the signals due to the exchangeable protons H_1 and H_3 in the ^1H spectrum: the spectrum of the aromatic protons passes into that of the AA′BB′ system, while the spectrum of protons 1–3 is transformed into the A_2B system. Because migration is intramolecular the multiplet character of the spectra does not disappear but is averaged out: e.g. the constant J_{AB} for the mean spectrum of type A_2B (protons 1–3) is $\frac{1}{2}(J_{12} + J_{23})$, where J_{12} and J_{23} are coupling constants for the instantaneous structure (XIVa).

The difficulties of calculating rate constants in strongly coupled spin systems with overlapping signals in the p.m.r. spectra can be avoided by using carbon-13 spectra. Under conditions of uncoupling from protons, splitting due to spin coupling with protons is absent from these spectra. It thus becomes possible to apply the Bloch–McConnell equations (Section II).

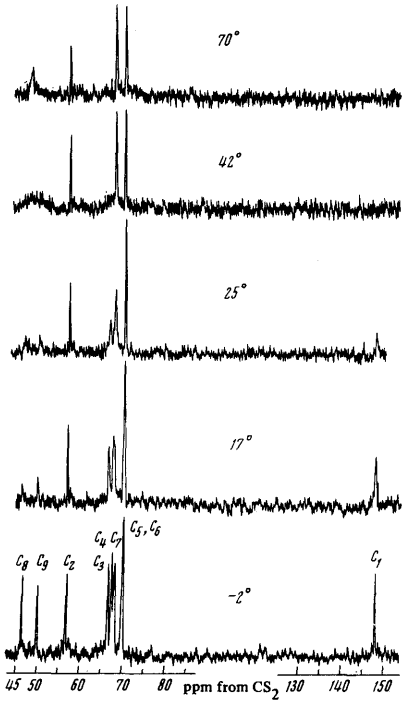


Figure 20. Carbon-13 n.m.r. spectra of trimethylstannylindene with uncoupling from protons at various temperatures[81].

Fig. 20 shows $^{13}C-\{^1H\}$ spectra (25.1 MHz) for trimethylstannylindene $C_9H_7Sn(CH_3)_3$ measured over a range of temperatures[81]. At room temperature (and below) the ^{13}C spectrum corresponds to the stereochemically rigid structure (XIVa). The assignment of the signals to individual carbon atoms is indicated on the spectrum (Fig. 20). Thanks to the absence of spin–spin interaction the exchange can at once be investigated for several pairs of

merging signals, viz. $C_{(1)}$–$C_{(3)}$, $C_{(4)}$–$C_{(7)}$, and $C_{(8)}$–$C_{(9)}$ (the signals from atoms $C_{(5)}$ and $C_{(6)}$ coincide in the limit of slow exchange). Comparison of experimental and theoretical spectral curves by line-shape analysis gives estimates of the activation functions for this process of $E_a = 13.8$ and $\Delta G^{\neq}_{300} = 15.3$ kcal mole^{-1}.

Fluctuating behaviour is of considerable theoretical interest, since it enables structural and kinetic features of certain molecular systems to be described from a single point of view. It may be supposed that d.n.m.r. spectroscopy will lead to the discovery of new classes of molecules of this type, and will enable quantitative aspects to be introduced into the construction of a theory of fluctuating behaviour.

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Laboratory of Nuclear Magnetic
Resonance, Chemistry Faculty,
Lomonosov Moscow State
University

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Problems of the Kinetics and the Topochemistry of Heterophase Copolymerisation

V.A.Myagchenkov and S.Ya.Frenkel'

The kinetics and the mechanism of binary heterophase copolymerisation are discussed by analogy with the differences in the kinetics and the statistics of homophase and heterophase polymerisation. The appearance of an interface, even in the absence of interphase interactions, leads to changes in the composition of the copolymer macromolecules and to departures in the overall process from the Mayo-Lewis canonical scheme even when r_A and r_B are constant. In order to record heterophase effects it is hence impossible to use the standard treatment of equilibrium diagrams or to estimate the mean compositions of the copolymers: the composition distribution functions must be analysed. Work is therefore discussed in which copolymerisation was conducted (wittingly or unwittingly) under heterophase conditions, practical criteria of heterophase character are examined, and its possible effects on the kinetics and the mechanism of the reaction are determined qualitatively. Possible methods for the quantitative analysis of copolymerising systems diverging from the general Mayo-Lewis scheme are also discussed. A list of 88 references is included.

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I. INTRODUCTION

The chief difficulties in the investigation of multicomponent systems arise from the need to allow for the contributions by individual components to the property or process studied. These difficulties can in principle be overcome if the contributions are additive. Then the calculated resultant functions describing the property or process (e.g. electrical conductivity, dielectric constant, heat capacity, entropy, optical density, etc.) usually agree well with the corresponding experimental quantities[1]. However, simple additivity is not satisfied by most multicomponent systems, which can be explained most generally by various types of interactions between the components influencing the magnitude and sometimes even the sign of the overall effect. In order to obtain the correct form or value of the resultant function it is necessary to introduce into the appropriate relations special parameters to allow for selective interactions between components, and these parameters should, of course, differ for different static or dynamic properties of the same multicomponent system. As a consequence, exact and detailed theories for specific resultant properties or processes have a limited sphere of application. In rare cases the unjustified extension of the limits of this sphere leads to fortuitous agreement between calculated and experimental values, but most often it yields erroneous results.

Special consideration will be given later to certain incorrect approaches in investigations of multicomponent copolymerising systems. Here we remark that, in the analysis of any polymeric systems, numerous additional complications arise connected with the nature of chain macromolecules, the special character of selective interactions, the presence together of different forms of polydispersity, etc.[2,3]. It is sufficient to recall that merely a change in molecular weight of a polymer component may cause a sharp change in the whole set of physicochemical properties of polymeric compositions and goods made from them[2]. Variation in composition of copolymers (inhomogeneity of composition) and the consequent spread of stable macromolecular conformations may lead to still greater uncertainty in the resultant physicochemical properties[4-6].

A typical example of complicated and ambiguous correlations between individual parameters in polymer systems is provided by the kinetics and the statistics of heterophase polymerisation[7,8]. Any specific and detailed theories (e.g. Stewart's theory of emulsion polymerisation) apply only to quite definite model system: outside the scope of such models, in application to workable processes of heterophase polymerisation, even qualitative use of the theories requires as a minimum careful preliminary investigation of the peculiarities of polymerisation in each specific system.

The situation is still more complicated with heterophase copolymerisation. The present stage of experimental work is hardly adequate for development of a general theory. Even use of the most general model of heterophase copolymerisation can yield only semi-quantitative agreement with experiment. And yet such a model is useful, since it will provide information on topochemical features of heterophase copolymerisation, on which the molecular-weight distribution and the inhomogeneity of composition largely depend. Furthermore, examples of the analysis of this model can show how aspects of heterophase processes *should not* be studied. It will later be shown in particular that application of the Mayo—Lewis scheme to the kinetics and the statistics of heterophase copolymerisation—and still more that of the Alfrey—Price "*Q—e*" scheme—may lead to errors even when the relative reactivities of the copolymers are independent of the reaction conditions.

II. GENERAL PROBLEMS OF THE ANALYSIS OF POLYMERISATION IN HETEROPHASE SYSTEMS

The interest of research workers in various forms of heterophase polymerisation is due primarily to the fact that they are usually easier and more convenient than homophase processes to conduct technically. Control of external (reactor) parameters is also easier with a heterophase than with a homophase process, and this at first glance widens the possibilities also of direct intervention in the kinetics, i.e. ultimately of controlling the physicochemical properties of the resulting polymer. It would be equally incorrect to underestimate or to overestimate these possibilities. Very much depends on the purpose of the polymer.

Let us consider a single example, in which the possibilities have perhaps been overrated. The emulsion polymerisation of vinyl acetate (a typical heterophase polymerisation[8]) is economically and technically more efficient than the so called "lacquer process", i.e. polymerisation in methanolic solution. If, however, the purpose of the process is to obtain *fibre-forming* poly(vinyl alcohol), all these advantages are completely levelled by the poor fibre-forming properties of the poly(vinyl alcohol) obtained in this way. As a result, the "lacquer" process exhibits greater overall efficiency. Nevertheless, the emulsion polymerisation of vinyl acetate must not be underrated if poly(vinyl acetate) itself is to be used as material in later stages, e.g. in emulsions employed in constructional engineering.

The principles of the statistical theory of heterophase homopolymerisation were set out by one of us elsewhere (Ref. 8, Chapter VI), and even brief mention of them is hardly required here. Therefore we shall merely consider those aspects of the theory and those approaches which are directly relevant to heterophase copolymerisation.

Let us first agree on terminology. The concepts of heterophase and heterogeneous polymerisation are by no means identical: heterogeneous polymerisation may be a homophase process, although the converse cannot apply. A heterogeneous system may in fact consist of two phases (e.g. a solid catalyst phase and a liquid monomer phase), but if chain growth and termination take place in only one phase, the process as a whole will be homophase. If, however, the elementary reactions of chain initiation, growth, termination, and transfer take place simultaneously at different rates in several coexisting phases, while interphase macromolecular reactions are possible (start of growth in one phase and continuation or completion in another phase, or bimolecular termination of chains growing in different phase, etc.), the process is heterophase[7,8]. The most characteristic indicator of a heterophase process is a multimodal molecular-weight distribution, in which the number of maxima shows a definite correlation with the number of intraphase and interphase mechanisms of termination of the kinetic chains. Henceforward we shall discuss only two-phase systems—not only because the difficulties of specific calculations increase disproportionately with increase in the number of phases but also because two-phase polymerising systems are most frequently met in practice.

Let us consider such a system consisting of phases I and II with any arbitrary distribution of components between these phases. Let the volumes of the phases be v_t^{I} and v_t^{II}, and the corresponding concentrations (in g cm^{-3} or g litre^{-1}) of monomer, initiator, and growing active centres (macroradicals in the case of radical polymerisation) M_t^{I} and M_t^{II}, I_t^{I} and I_t^{II}, and $\cdot R_t^{I}$ and $\cdot R_t^{II}$ respectively. We denote the concentrations of other components that may influence the kinetics and the mechanism of polymerisation by

$$\lambda_{1t}^{I}, \lambda_{1t}^{II}, \lambda_{2t}^{I}, \lambda_{2t}^{II} \ldots \lambda_{it}^{I}, \lambda_{it}^{II} \ldots \lambda_{kt}^{I}, \lambda_{kt}^{II}.$$

These components may be inhibitors, sensitisers, modifiers, chain-transfer agents, etc. The concentration ratios of individual components in phases I and II can in principle be varied over the ranges

$$0 \leqslant I_t^{I}/I_t^{II} \leqslant \infty,\ 0 \leqslant M_t^{I}/M_t^{II} < \infty,\ 0 \leqslant \frac{R_t^{I}}{R_t^{II}} < \infty,\ 0 \leqslant \frac{\lambda_{it}^{I}}{\lambda_{it}^{II}} < \infty \quad (i = 1, 2, 3 \ldots k).$$

In this notation the condition of "homophasicity" is formulated as the simultaneous approach by the ratios for M and R· to 0 or ∞; the condition of "diphasicity", on the other hand, requires that these ratios should be finite. The ratios of other concentrations have no decisive significance for the "phasicity" of the process. These conditions reflect the quite trivial fact that a heterogeneous system is not a sufficient criterion that polymerisation shall be a heterophase process.

All types of two-phase polymerisation (whether emulsion, suspension, or gas-phase polymerisation, in a precipitant, or the block polymerisation of monomers that are not solvents for their polymers) are characterised by the presence of an interface of area S_t. In the simplest form of steady-state process polymerisation occurs independently in phases I and II. This means that at time t the laws of polymerisation in phase I are determined unambiguously by the values of M_t^{I}, I_t^{I}, $\cdot R_t^{I}$, and λ_{it}^{I} ($i = 1, 2, \ldots, k$) and are independent of M_t^{II}, I_t^{II}, $\cdot R_t^{II}$, and λ_{it}^{II}. With "I" and "II" interchanged the same applies to phase II. The ratios

$$\frac{M_t^{I}}{M_t^{II}},\ \frac{R_t^{I}}{R_t^{II}},\ \frac{I_t^{I}}{I_t^{II}},\ \frac{\lambda_{it}^{I}}{\lambda_{it}^{II}},$$

depend indirectly on S_t, being determined in the simplest case by Langmuir's law. It is assumed that the contraction in each phase can be neglected, and also that the dimensions l of individual units (aggregates, drops, etc.) constituting the phases are large in comparison with those of the individual macromolecules.

Under these conditions it is reasonable to expect, at least for not too large degrees of conversion Ψ, that the chief laws of homophase polymerisation will be obeyed within phases I and II, e.g. that the overall rate of the process will be proportional to $(I_t^{I})^{\frac{1}{2}}M_t^{I}$ and $(I_t^{II})^{\frac{1}{2}}M_t^{II}$ in the respective phases. Resultant kinetic curves or molecular-weight distributions for such a heterophase system can be calculated simply by superposing corresponding curves for phases I and II.[8]

In order to obtain information on the parameters of interaction between the phases it is necessary to obtain data on the kinetics and the molecular-weight distribution in each phase for various degrees of conversion. This alone requires a large number of delicate experiments involving the separate study of polymerisation each phase. Amongst such important parameters controlling the process are firstly the time relations $M^{I}/M^{II} = f_1(t)$, $I^{I}/I^{II} = f_2(t)$, $\cdot R^{I}/\cdot R^{II} = f_3(t)$, and $\lambda_i^{I}/\lambda_i^{II} = f_{4,\,i}(t)$, secondly the physicochemical characteristics of the interfacial layers, and thirdly the kinetic parameters of all types of chemical reactions and mass exchange in the boundary layers.

Separate observation of the processes in phases I and II is possible only by use of the most recent methods, in particular optical (e.g. luminescent) or radioactive "labels"; in some systems the phases can be separated artificially by means of a preparative ultracentrifuge[9]; and in principle more standard optical methods can be used to determine M_t^I (or M_t^{II}), at least in one of the phases. Promising experiments have also been made on the principle of "intervention", when polymerisation in one phase is artificially suppressed (e.g. by introducing into the system an inhibitor soluble only in this phase).

On the other hand, use of certain favourite routine methods (e.g. dilatometry) for these purposes is by no means always possible, for the coefficients of contraction K^I and K^{II} in the two phases are not equal in many systems with interacting phases. (We recall that $\Delta v^I = K^I(M^I_{t=0} - M^I_t)$ and $\Delta v^{II} = K^{II}(M^{II}_{t=0} - M^{II}_t)$, where Δv^I and Δv^{II} are the changes in volume of the phases at degrees of conversion of Ψ^I and Ψ^{II}.) Hence the overall change in volume of the system is not proportional to $\Psi^I + \Psi^{II}$, and dilatometry does not give a quantitative measure even of the overall process.

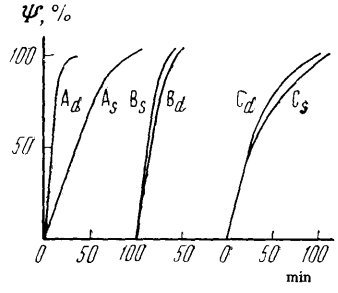


Figure 1. Dependence of degree of conversion Ψ on time in the heterophase (*d*) and homophase (*S*) polymerisation[13] of: A) acrylonitrile; B) vinyl chloride; C) vinylidene chloride—acrylonitrile system.

It appeared at one time that the main features of the most thoroughly investigated type of heterophase polymerisation—emulsion polymerisation—would be explained by Smith and Ewart's theory[10,11], which postulated that the emulsified particles were constant in number and merely underwent an increase in volume with increase in degree of conversion. However, later work by Medvedev and his collaborators showed that this theory paid insufficient attention to the role of the interface in the general reaction scheme. They showed in particular that the overall rate of polymerisation may be proportional either to the square root or to the first power of the concentration of the emulsifier according to whether the latter is soluble or insoluble in water. However, even Medvedev's theory gives quantitative agreement with experiment in by no means all cases. Only semi-quantitative agreement is obtained when calculated and experimental kinetic curves are compared[12]. As Kargin correctly remarked in his plenary report to a conference on emulsion polymerisation in Odessa in 1969, the theoretical problems of emulsion polymerisation are far from being exhausted, and more specialised experimental work must be undertaken with the development of new, improved theories.

A few specific examples will demonstrate the complications, in interpreting kinetic or statistical features of polymerisation, that arise from the two-phase character of the process. Fig. 1 compares kinetic curves for the homophase and heterophase polymerisation and copolymerisation of certain vinyl monomers. With vinyl chloride or in the copolymerisation of vinylidene chloride with acrylonitrile the change from a homophase to a heterophase process is not accompanied by significant change in the rate of polymerisation. With vinyl chloride the appearance of a new phase leads to some slowing down of the process, but in copolymerisation the appearance of a second phase results, on the contrary, in some acceleration. Nevertheless, the polymerisation of acrylonitrile is far more rapid in a two-phase system. Such relations between reaction velocity and nature of reaction medium can be explained only on the basis of the effective concentrations of monomers and initiator in phases I and II. The presence of several components often has the effect (especially in emulsion polymerisation) that slight changes in external conditions or small additions may change substantially the situation in the boundary layers and hence cause a shift in equilibrium in the system. This is clearly evident in Fig. 2, illustrating the effect of additions of various amines on the degree of conversion in the emulsion polymerisation of butadiene[14].

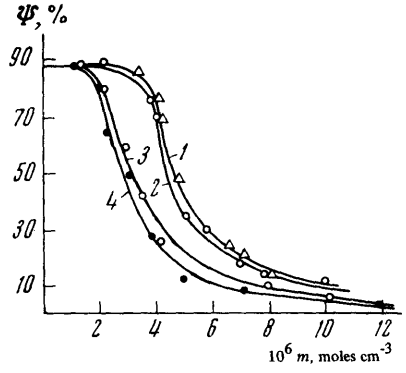


Figure 2. Dependence of degree of conversion Ψ in the emulsion polymerisation of butadiene[14] at pH 3.4 and 70°C for 24 h on the concentration *m* of amines: 1) propylamine; 2) butylamine; 3) hexylamine; 4) octylamine.

In this connection interesting results have been obtained[15,16] on the effect on the rate of emulsion polymerisation of which phase the surface-active agent is introduced into. The thickness of the surface layer in the emulsion polymerisation of vinyl acetate limits diffusion of the monomer[16]. In several cases a surface-active agent affects the rate of breakdown of the initiator, and hence the rate of polymerisation[17-19]. In such systems a definite sequence in the arrangement of monomer units may be expected in the surface layer. Under certain favourable conditions this in turn will enable us to influence not only the overall rate of the process but also the

fine structure of the chain by varying the emulsifier concentration.

When an emulsifier—activator is used, the rate of the process, the particle size of the disperse phase, the fine structure, and the molecular-weight distribution are greatly affected by the pH. Significantly different rates of emulsion polymerisation are obtained by the use of oligomeric or polymeric emulsifiers of fixed molecular weight but with different contents of ionogenic groups[20]. These differences were attributed to the size and shape of the chain molecules forming the boundary layer; these characteristics depend in turn on the concentration of ionogenic units in the chain[21].

Overenthusiasm for polymeric emulsifiers or emulsion stabilisers is dangerous. When poly(vinyl alcohol) of low molecular weight is used in the emulsion polymerisation of vinyl acetate, for example, the resulting polymer is almost completely unsuitable for the production of poly(vinyl alcohol), both because of the wide multimodal molecular-weight distribution and because of the enhanced degree of branching: the polymeric component of the emulsifier has an unfavourable effect on the balance of secondary reactions (Ref. 8, Chapter III).

On the whole, work published recently (that cited here can be supplemented by two papers by Enikolopyan and his coworkers[22,23]) confirms the fundamental principles that follow from the statistical consideration of heterophase processes. Significant progress in the corresponding experimental investigations will require more intense development of specific methods of the type mentioned in this Section.

III. TWO-PHASE COPOLYMERISATION AND LIMITS OF APPLICABILITY OF MAYO—LEWIS SCHEME

The kinetics of the binary radical copolymerisation of monomers A and B are determined by the four elementary reactions of chain growth

$$\begin{aligned} &A_{n-k-1}B_k\dot{A} + A \xrightarrow{k_{AA}} A_{n-k}B_k\dot{A} \\ &A_{n-k-1}B_k\dot{A} + B \xrightarrow{k_{AB}} A_{n-k}B_k\dot{B} \\ &A_{n-k-1}B_k\dot{B} + B \xrightarrow{k_{BB}} A_{n-k-1}B_{k+1}\dot{B} \\ &A_{n-k-1}B_k\dot{B} + A \xrightarrow{k_{BA}} A_{n-k-1}B_{k+1}\dot{A} \end{aligned} \qquad (1)$$

where $A_{n-k-1}B_kA\cdot$ and $A_{n-k-1}B_kB\cdot$ are macroradicals consisting of n repeating units with A and B terminal units respectively. It is supposed that $1 \leqslant k < n-1$, while the symbols B_0 and A_0 simply denote the absence of these units in the macroradical chains. The elementary reactions have the rate constants k_{AA}, k_{AB}, k_{BB}, and k_{BA} respectively. We shall further assume that the usual quasi-stationary conditions are satisfied, i.e. that the rates of initiation comprising the elementary reactions

$$I \longrightarrow 2\dot{R},\ \dot{R}+A \xrightarrow{k_u} R\dot{A};\ \dot{R}+B \xrightarrow{k_u'} R\dot{B},$$

in which the notation is self-evident, and of termination of the kinetic chain by recombination or disproportionation

$$A_{n-k}B_k\dot{A} + A_{n'-k'}B_{k'}\dot{B} \begin{cases} \xrightarrow{k_0} A_{n+n'+1-k-k'}B_{k+k'+1} \\ \xrightarrow{k_0'} A_{n-k+1}B_k + A_{n'-k'}B_{k'+1} \end{cases}$$

are far smaller than the rate of chain growth:

$$k_u + k_u' + k_0 + k_0' \ll k_{AB} + k_{AA} + k_{BB} + k_{BA}. \qquad (2)$$

Proceeding from these hypotheses Mayo and Lewis[24]—almost simultaneously with Wall[25] and also Alfrey and Goldfinger[26]—deduced a relation between the four growth rate constants, the composition of the initial monomer mixture (substrate), and the composition of the macromolecules formed. If m_A and m_B are the molar concentrations of monomers A and B in the substrate, while M_A and M_B are the molar concentrations of the components in the copolymer ($m_A + m_B = 1$ and $M_A + M_B = 1$), we have

$$\frac{M_A}{M_B} = \frac{m_A}{m_B}\,\frac{r_A m_A + m_B}{r_B m_B + m_A} \qquad (3)$$

in which $r_A = k_{AA}/k_{AB}$ and $r_B = k_{BB}/k_{BA}$. On passing to concentrations by weight we have

$$g\,\frac{\alpha_A(1-\beta_A)^2}{(1-\alpha_A)\beta_A^2}\,r_B - r_A = \frac{1-\beta_A}{\beta_A}\left(g - \frac{\alpha_A}{1-\alpha_A}\right) \qquad (4)$$

where β_A and α_A are the weights of component A in the substrate and in the copolymer respectively, and g is the ratio of the molecular weights of A and B.

The deduction of Eqns. (3) and (4) was based on five assumptions: (i) the ensemble of copolymer molecules contained no oligomers (in the true meaning of this word); (ii) both r_A and r_B were constant, so that the relative reactivities did not depend on the nature of the penultimate and more remote units; (iii) the degree of conversion was so small ($\leqslant 0.03$) that both β_A and m_A/m_B could be regarded as constant; (iv) growth reactions were completely reversible; and (v) the reaction system was homogeneous at all degrees of conversion.

Integrating (3) and passing to the relations $M_A/M_B = F(m_A/m_B, r_A, r_B)$ for $\Psi > 0.1$, we then obtain[27,28]

$$\lg\frac{(m_A)_t}{(m_A)_{t=0}} = \frac{r_A}{1-r_A}\lg\left(\frac{m_A}{m_B}\right)_{t=0}\cdot\left(\frac{m_B}{m_A}\right)_t - \frac{1-r_Ar_B}{(1-r_A)(1-r_B)}\lg\frac{(r_B-1)\left(\frac{m_B}{m_A}\right)_t - r_A + 1}{(r_B-1)\left(\frac{m_B}{m_A}\right)_{t=0} - r_A + 1}. \qquad (5)$$

All this work is quite well known. Equations (3)—(5) enable "copolymerisation constants" r_A and r_B to be found from known relations between the composition of the copolymer and that of the substrate. However, what is today called the "Mayo—Lewis scheme" and is used, often thoughtlessly, for the quantitative description of binary copolymerisation is quite different from the original theses[24]. Exaggerating somewhat, we can divide the "scheme" (all in today's interpretation) into the fundamental postulate and the actual scheme. The postulate states that r_A and r_B are actually copolymerisation *constants*, depending neither on the degree of conversion nor on the fine structure of the growing chain end. The actual scheme includes, besides the fundamental postulate, the above five principles, with the automatically satisfied quasi-stationary condition.

However, Mayo and Lewis emphasised the arbitrariness of this scheme. With regard to the fundamental postulate, they spoke in general not of copolymerisation "constants" but of activity ratios, which is far more to the point. It is necessary in principle to take into account the possible effect on these ratios of the fine structure of the chain end, i.e. the influence of the nature of penultimate and more remote units (this aspect has since been examined in detail in a series of papers by Ham and his coworkers). Nor can special modes of copolymerisation be excluded, in which the activity ratios change during the process

(these questions have already been reviewed in detail[31], so that here we shall be only incidentally concerned with them).

A roughly similar situation is found with the actual scheme. Even when the fundamental postulate is satisfied, the scheme as a whole may diverge sharply from the "canonical conditions" with non-observance of principle (v). Again, as early as the 1940s papers by Mayo[24], Ham[29], and Smith[30] specially stipulated that the appearance of phase heterogeneity in a system may cause strong departures from the laws of a homophase process, when it becomes problematical whether Eqns. (3)—(5) are satisfied. These papers were developed in later publications by Mayo and Ham (see monograph[27]). Even the observance of quasi-stationary conditions is complicated in two-phase systems (Ref. 8, Chapter VI).

Nevertheless, the number of publications in which the authors use the "Mayo—Lewis scheme", without settling the question of its applicability to the specific process, is continually increasing. We have already noted[31] that this is explained to some extent by the fact that the processing of experimental data in the form $M_A/M_B = F(m_A/m_B)$ by means of Eqns. (3)—(5) is not "self-checking", for it is relatively insensitive to the appearance of any anomalies in the copolymerisation.

It was shown experimentally[32] that the presence of polytetrafluoroethylene affects the composition of the macromolecules formed by the copolymerisation of styrene (A) with acrylonitrile (B) even at $\Psi < 0.03$, which was explained by selective solvation of the monomers on the polytetrafluoroethylene surface. On addition of a precipitant the transition to heterophase conditions of copolymerisation was accompanied by the appearance of macromolecules differing in composition from that calculated by means of formula (3) with values of r_A and r_B for the homophase process. Ryabov et al.[33,34] obtained products differing in composition by the block and by the suspension copolymerisation of methyl methacrylate (A) with methacrylic acid (B): in the block $r_A = 0.35 \pm 0.01$ and $r_B = 1.63 \pm 0.12$, but in suspension copolymerisation $r_A^* = 0.63 \pm 0.02$ and $r_B^* = 1.07 \pm 0.13$ (here and subsequently an asterisk (*) will mean that the quantity has been obtained by the formal application to a heterophase process of relations valid for the homophase process). These workers established that during suspension copolymerisation the copolymer is enriched in component A, the effect increasing with dilution of the suspension, which may be explained by preferential dissolution of component B in water, and thus be decrease in the effective concentration of methacrylic acid in the reaction zone.

Plate and Uzhinova[35] found that, in the copolymerisation of styrene (A) with methyl methacrylate (B) initiated by an activated sodium chloride surface, the values of $r_A^* = 1.40$ and $r_B^* = 0.30$ obtained did not correspond to the values $r_A = 0.46$ and $r_B = 0.52$ for the homogeneous process. This difference is especially significant because, in contrast to homogeneous copolymerisation, the system with the first pair of values has no azeotropic point. These results were explained by preferential adsorption of styrene on the sodium chloride surface, which they relate to features of the electronic interaction between the styrene radical and the surface. A transition from a system with an azeotropic point to one without it has been shown for the copolymerisation of methyl methacrylate (A) and methacrylic acid (B): in dioxan $r_A = 0.96 \pm 0.50$ and $r_B = 0.19 \pm 0.06$; in water (heterophase process) $r_A^* = 5.80 \pm 0.50$ and $r_B^* = 0.15 \pm 0.06$.

If, however, calculations are based on true monomer concentrations in the reaction zone, the heterophase copolymerisation conforms to the "classical" scheme in cases in which the fundamental postulate holds. This has been shown e.g. in the radiation gas-phase copolymerisation of acrylic acid and styrene on a polypropylene fibre[36], when r_A and r_B were calculated from the true concentrations of the monomers in the reaction zone. The necessity of allowing for the redistribution of monomer concentrations in two-phase copolymerisation has been pointed out also by one of us (Ref. 8, Chapter VI) in a discussion of certain features of the polymerisation of acrylonitrile in aqueous dispersion and the block copolymerisation of methyl methacrylate and methacrylic acid.

Herma[37] notes a change in the (apparent) relative reactivity on passing from homophase to heterophase systems in the case of the copolymerisation of acrylonitrile with acrylic and methacrylic acids in the mass, in dimethyl sulphoxide, and in other solvents. Roskin et al.[38] find relative reactivities to be unchanged on passing from a homophase to a two-phase system in the copolymerisation of methylallyl chloride with acrylonitrile. They reach the same conclusion in an investigation of the copolymerisation of acrylonitrile (A) with allylic amines (B) in a block, in benzene (heterophase process), and in dimethyl sulphoxide (homophase process)[39]. The constants Q and e in the Alfrey—Price equation were calculated from the values obtained for r_A^* (with r_B^* equated to zero). In a slightly later paper[40] on the copolymerisation of acrylonitrile (A) with bicyclo[2,2,1]heptenedicarboxylic acid and its anhydride in various media these workers give values for r_A^* (always on the assumption that $r_B = r_B^* = 0$): in benzene 3.36 ± 0.37 from analytical data for nitrogen and 3.51 ± 0.35 in radioactive tracer experiments; in dimethylformamide $r_A = 3.63 \pm 0.31$; in the mass $r_A^* = 3.41 \pm 0.41$; in water $r_A^* = 2.02 \pm 0.38$; and in aqueous sodium thiocyanate $r_A = 3.81 \pm 0.31$. For certain points the formal application of the Mayo—Lewis equations gave the definitely absurd results (as pointed out by the authors themselves) of $r_A^* < 0$.

In the copolymerisation of acrylonitrile with salts of allylamines and methylallylamines[40,41] r_A^* and r_B^* are independent of the degree of conversion, but on the other hand depend on the dielectric constant of the medium (copolymerisation was conducted in the mass, in benzene, and in water). It was also found that $r_A^* \neq r_A$ and $r_B^* \neq r_B$, where r_A and r_B were determined for the homogeneous process (in dimethylformamide and in dimethyl sulphoxide)[42].

The pH dependence of the composition of vinyl acetate—acrylonitrile copolymers is attributed[43] to redistribution of the concentrations of the two monomers on particles of the resulting copolymer.

Bender[44] studied the copolymerisation of butadiene (I) with vinyl (II), isopropenyl (III), and α-phenylvinyl (IV) acetates in an emulsion. Copolymerisation in the I—II and I—III systems gives low yields, and the copolymer macromolecules contain small quantities of components II and III. Copolymerisation in the I—IV system goes to considerably higher degrees of conversion, which was explained by enhanced resonance stabilisation of α-phenylvinyl acetate (in comparison with the monomers II and III) due to the α-phenyl group.

Korshak et al.[45] have investigated the copolymerisation of butadiene with isopropenylcarborane at high temperatures. They find differences in the kinetics of the process

and in the compositions of the macromolecules formed compared with the heterophase emulsion copolymerisation of the same monomers.

Brandrup[46] finds that the copolymerisation of acrylonitrile with acrylates in solution and in emulsion yields macromolecules differing significantly in composition.

Japanese workers[47] investigated the heterophase copolymerisation of vinyl chloride with ethylene with and without the addition of 30% aqueous silver nitrate solution. Enrichment of the copolymer with ethylene in the former case was explained by formation of a complex of ethylene with silver nitrate.

Investigation of the copolymerisation of methyl methacrylate with acrylonitrile, acrylic acid, and vinylidene chloride and of vinylidene chloride with acrylonitrile in a precipitant medium (cyclohexane) showed[48] that the kinetics of the process and the composition of the resulting macromolecules were influenced by the nature of the interface.

A study[49] of the copolymerisation of vinyl acetate (A) with diallylcyanamide (B) in an emulsion gave $r_A^* = 0.6$ and $r_B^* = 1.62$. During copolymerisation the monomer B underwent internal cyclisation to form piperidine rings in the framework of the macromolecular chain of the copolymer.

The copolymerisation of acrylonitrile with vinyl sulphone dyes in various solvents is a heterophase process[50], and the composition of the copolymer depends on the physicochemical properties of the solvent.

Ivanov et al.[51] investigated the kinetics of the copolymerisation of 2,3-bisdiethylphosphinobuta-1,3-diene with butadiene and isoprene in the presence of water as catalyst. They give data on the effect on the kinetics of the concentration of water, the composition of the substrate, the pH, and the degree of conversion. Although the separate monomers are incapable of homopolymerisation under the same conditions, copolymerisation is quite rapid, and the composition of the copolymers depends on that of the substrate. The composition data for this heterophase copolymerisation were processed on the basis of the "classical" Mayo—Lewis scheme.

A comparison of the kinetics and the chemical composition of the macromolecules in the homophase and heterophase copolymerisation of acrylonitrile with sodium ethylenesulphonate in aqueous medium at various pH values and in dimethyl sulphoxide achieved the transition from homophase to heterophase process by varying the composition of the initial monomer mixture[52,53]. Later Izumi[54] assessed the effect of the reaction medium on the copolymerisation of acrylonitrile (A) with methyl acrylate in solution (with dimethyl sulphoxide as solvent), in emulsion, and in suspension. The composition of the copolymer for $\Psi < 0.08$ was determined by infrared spectroscopy, by high-resolution nuclear magnetic resonance, and also by analysis for nitrogen. For homophase copolymerisation in dimethyl sulphoxide $r_A = 1.02 \pm 0.02$ and $r_B = 0.70 \pm 0.02$, with heterophase copolymerisation in an emulsion $r_A^* = 0.78 \pm 0.02$ and $r_B^* = 1.04 \pm 0.02$, and in suspension $r_A^* = 0.75 \pm 0.02$ and $r_B^* = 1.54 \pm 0.02$. Tacitly assuming that the "canonical" Mayo—Lewis scheme applied to all the processes investigated, these workers explained the differences in the values of r_A, r_A^* and r_B, r_B^* in terms of the *effective* concentrations of monomers A and B near the macroradical. In the case of suspension copolymerisation it was supposed that the concentration of the sparingly water-soluble methyl acrylate was higher in the dispersed particles than in the substrate. In the case of emulsion copolymerisation the process occurred both in the micelles and in the aqueous phase, which was regarded as explaining the intermediate values of r_A^* and r_B^* in the emulsion, between r_A and r_B in solution and r_A^* and r_B^* in suspension. The Alfrey—Price parameters were calculated from the values found for r_A and r_B as $Q_1 = 0.60$ and $e_1 = 1.2$ for acrylonitrile, and $Q_2 = 0.29$ and $e_2 = 0.62$ for methyl acrylate.

Rafikov et al.[55] found that the copolymerisation of aryldichlorophosphines with butadiene may be either homophase or heterophase depending on the composition of the substrate. Table 1 gives copolymer compositions for various substrate compositions. Careful analysis of these results indicates that formulae (3)—(5) cannot be used to describe the dependence of m_2/m_1 on M_2/M_1. The kinetics of copolymerisation in this system will be discussed later.

Table 1. Composition data for copolymers of aryldichlorophosphines (A) with butadiene (B).

Composition of initial mixture of monomers		Ψ, %	Composition of copolymer	
M_A	M_B		m_A	m_B
Ar = C_6H_5				
0.05	0.95	28.8	0.35	0.65
0.10	0.90	37.8	0.45	0.55
0.20	0.80	8.5	0.54	0.46
0.30	0.70	12.5	0.43	0.57
0.40	0.60	11.7	0.50	0.50
0.50	0.50	19.4	0.54	0.46
Ar = $CH_3.C_6H_4$				
0.05	0.95	25.3	0.51	0.49
0.10	0.90	35.8	0.48	0.52
0.20	0 80	13.1	0.50	0.50
0.30	0.70	13.4	0.49	0.51
0.40	0.60	13.8	0.48	0.52
0.50	0.50	13.4	0.52	0.48
Ar = ClC_6H_4				
0.05	0.95	28.3	0.46	0.54
0.10	0.90	27.2	0.52	0.48
0.20	0.80	7.05	0.55	0.45
0.30	0.70	6.14	0.50	0.50
0.40	0.60	6.20	0.56	0.44
0.50	0.50	5.05	0.53	0.47
0.60	0.40	4.68	0.55	0.45

Fig. 3 shows composition diagrams[56] for the copolymerisation of methacrylic acid (A) with phenyl methacrylate (B) in benzene alone and mixed with dimethylformamide, the latter at a constant ratio to component A of 3:1. It was found that in benzene $r_A^* = 0.40 \pm 0.14$ and $r_B^* = 0.59 \pm 0.17$, but in its mixture with dimethylformamide the corresponding ratios were 0.21 ± 0.02 and 1.52 ± 0.13. Although r_A^* and r_B^* were assumed to describe the process quite unambiguously, it seems to the Reviewers that the results do not fit the Mayo—Lewis scheme, and this difference in opinion is not merely a matter of taste. In the former case (benzene) departures from the scheme would be due to the heterophase character of the process, but in the latter the relative reactivities of the monomers may actually depend on the benzene : dimethylformamide ratio.

A very interesting study was made by Kargin et al.[57] of the copolymerisation of potassium acrylate (A) with acrylamide as a homophase process initiated by ultraviolet

radiation and hydrogen peroxide and as a heterophase process initiated by hydrogen peroxide in the presence of magnesium oxide or of lead chromate and sodium thiosulphate. In the heterophase copolymerisation enrichment of the copolymer with component A was observed, and was explained by preferential adsorption of potassium acrylate at the solid interface (Fig. 4). Potentiometric titration of the copolymers gave especially interesting results (salt groups in the copolymer had first been converted into acid groups by treatment with hydrochloric acid). With the same mean composition $pK_1 = 4.4597$ in the case of heterophase copolymerisation, but $pK_2 = 4.2760$ in the homophase process. The incontrovertible conclusion was reached that the high value of $\Delta pK = 0.1837$ indicates a significant difference in fine structure between the copolymers obtained under different conditions. Evidence of this is provided also by the pH dependence of the specific viscosity and also directly by the potentiometric titration curves themselves (Fig. 5). A difference in fine structure at the same mean composition implies, of course, a difference in magnitude and character of the inhomogeneity of composition, which is greater in the heterophase than in the homophase process.

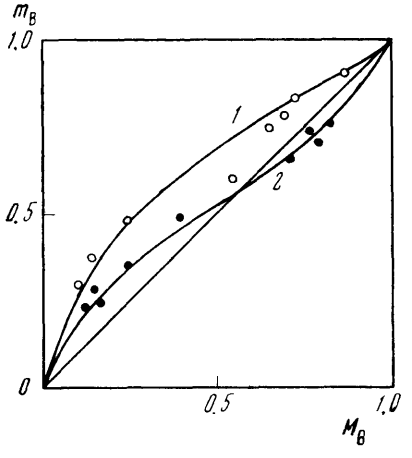


Figure 3. Composition diagrams for the copolymerisation of methacrylic acid (A) with phenyl methacrylate (B) in: 1) benzene–dimethylformamide mixture; 2) benzene.

Here it is opportune to recall certain characteristic differences between the statistical distribution of composition in a copolymer and the molecular-weight distribution in a homopolymer. The molecular-weight distribution is defined unambiguously by a *single* function. One function is, strictly speaking, insufficient for the heterogeneity of composition. The analogue of the molecular-weight distribution is the composition distribution discussed in a previous review[31]. In this case a set of linear chains of the same degree of polymerisation is characterised by their *composition*, not by their fine structure. The fine structure is the second characteristic of heterogeneity of composition. To make clear what we are talking about, we now imagine a set of linear chains having the *same composition* (and also degree of polymerisation, of course). Two limiting fine structures are possible: the alternant copolymer ABABABABABAB... can be regarded as a homopolymer with AB as the repeating unit; the other limiting structure is the block copolymer AAAAAAAA... BBBBBB... . All intermediate forms, while having the same composition (not the mean but the true composition!), will differ in fine structure, i.e. in the distribution of units along the chain†. The fine structure will affect the physicochemical properties of the macromolecules not a whit less—and in many cases more—than will the mean composition.

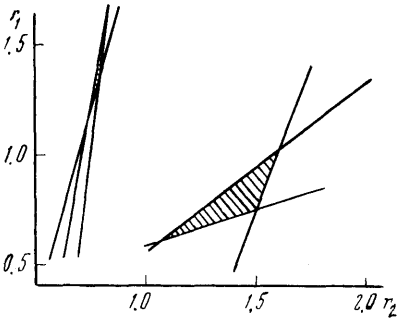


Figure 4. Relative reactivities of potassium acrylate (r_1) and acrylamide (r_2) in homophase and heterophase copolymerisations[57].

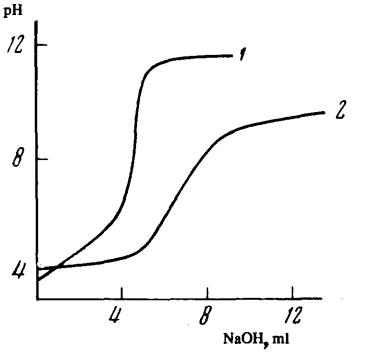


Figure 5. Potentiometric titration curves for saponified copolymers of potassium acrylate and acrylamide having the same composition but obtained by: 1) heterophase copolymerisation; 2) homophase copolymerisation[57].

Supplementing the work cited above[57] we may mention the difference in properties between copolymers of methyl methacrylate and methacrylic acid of the same mean composition obtained by the usual random copolymerisation and by saponification of poly(methyl methacrylate) respectively. In the former case reactivity ratios "work", and

† In conformity with the terminology adopted the distribution of macromolecules having the same composition but differing in fine structure is characterised by the *configurational heterogeneity* function.

the fine structure can be identified by the distribution in the chain of dyads, triads, tetrads, etc. of one of the components, which, of course, depends on the true values r_A and r_B (or their mean values, if they vary with the degree of conversion). In the latter case the fine structure can be characterised in the same way, but the distribution will be purely accidental. In "neutral" solvents like ethyl acetate or dichloroethane such copolymers form "vulcanised" (by hydrogen bonds) molecular loops. A single methacrylic-acid group, a dyad, and a triad are obviously equally effective in forming a "vulcanisation" bond with some distant unit along the chain. But this implies that the efficiency of "ultilisation" of the carboxyls is considerably higher with an absolutely random distribution of units: in a triad, for example, two units are "unemployed". This is shown in the average number of intrachain hydrogen bonds and hence in the tightness of the coil, which can easily be determined e.g. viscometrically.

One of the first qualitative predictions of differences in fine structure between homophase and heterophase copolymerisation based on the "Langmuir" approximation was made in an analysis of the copolymerisation of acrylonitrile with vinyl monomers in aqueous dispersion (Refs.39, 38, and 8, Chapter VI). Because of the redistribution of monomer concentrations in solution and on the surface of the growing polymer particles, with interphase recombinations occurring, the fine structure of the "heterophase" copolymer should contain blocks varying in mean composition.

Quite recently Japanese workers[58] have obtained a similar result directly in the heterophase copolymerisation of acrylonitrile with methyl methacrylate in hexane. The composition of the copolymer inside the deposited particles differed appreciably from that of the macromolecules obtained in homogeneous systems. Since the degree of conversion in this work was sufficiently large (>0.05), the variation with Ψ was allowed for in calculating the theoretical mean composition α.

In a paper mentioned already[51] and also in the more detailed account of this work[59] values of r_A^* and r_B^* were calculated, and the composition of the resulting copolymers was found to depend on the accessibility of the polymerising system to atmospheric oxygen.

IV. SIMPLIFIED MODELS OF HETEROPHASE COPOLYMERISATION

In this Section we try to use model systems, free from additional complications, firstly to establish experimental criteria of the applicability of the canonical Mayo—Lewis scheme to the description of heterophase copolymerisations, and secondly to compare the level of information obtained by determining the mean composition of copolymers and analysing composition distribution curves.

We consider an idealised system[60] in which a transition can occur from homophase to heterophase copolymerisation or conversely. Such a system comprises a pair of monomers having upper and lower consolute temperatures T_{1c} and T_{2c} within a relatively narrow temperature range. Copolymerisation is assumed to be possible both in regions of complete miscibility and between T_{1c} and T_{2c} (Fig. 6). We quite deliberately ignore one of the chief complications that always arise in reality—the appearance of the copolymer, which itself may affect the "phasicity" of the process, as well as the variation in concentration of the comonomers—and assume that the copolymer leaves the reaction zone. The position of the copolymerising system on the phase diagram (Fig. 6) will then be determined solely by the concentrations of unconsumed monomers and by the temperature. With this reservation, the following modes of copolymerisation are possible.

1. Isothermal copolymerisation at constant temperature T_3. We assume the volume of phases I and II to be fixed; $\beta = \beta_3'$ and β_3'' in phases I and II; and both r_A and r_B are constant.

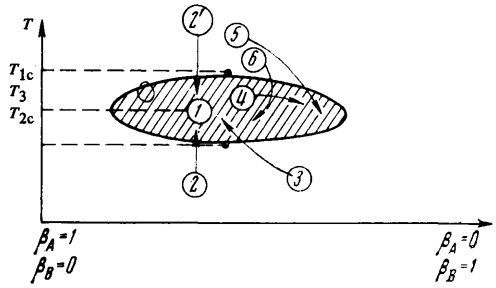


Figure 6. Equilibrium diagram of simplified schemes for the heterophase copolymerisation of partly miscible monomers. The hatched area represents separation of the system into two phases. The numbering corresponds to the models in the text. Models 1, 2, and 2′ are azeotropic processes, with the composition of the substrate remaining unchanged. In the more complicated models 3—6 the arrows indicate the variation in composition of the substrate during copolymerisation. The main explanations will be found in the text.

2. Non-isothermal copolymerisation beginning either below T_{2c} or above T_{1c}, then continuing with rise or fall in temperature respectively, and emerging into the region of phase separation, which occurs at a critical degree of conversion Ψ_c. When $\Psi < \Psi_c$ the process is homophase; when $\Psi \geq \Psi_c$ it is heterophase. We ignore interaction between the phases, and assume as before that both r_A and r_B are constant.

3. A variant of models *1* and *2* complicated by dependence of r_A and r_B on temperature or (alternatively) substrate composition. Interaction between the phases is neglected.

4. A two-phase process from the start, with both r_A and r_B constant. Interaction does occur between the phases, and in the simplest form can be reduced to variation in the volumes v^I and v^{II} and in the compositions β_A^I and β_A^{II} (as a result of mass exchange).

5. Model similar to *4*, but the two-phase process begins at $\Psi = \Psi_c$.

6. Additional complications in comparison with models *4* and *5*, caused by the dependence of the reactivity ratios on temperature and substrate composition: $r_A = r_A(T, \beta)$ and $r_B = r_B(T, \beta)$.

Quantitative treatment of models *4*—*6* requires that definite parameters should be specified for the interaction between phases I and II, which involves fundamental difficulties in attempts to allow for the specific limits of separation on variation of components A and B in the phases. Thus even with the above oversimplifications

(neglect of the effect of the copolymer formed) actual calculations can easily be completed only for the most primitive models *1* and *2*. The analytical expression[61]

$$1-\Psi=\left(\frac{\beta_A}{\beta_A^0}\right)^{\frac{r_B}{1-r_B}}\left(\frac{1-\beta_A}{1-\beta_A^0}\right)^{\frac{r_A}{1-r_A}}\left\{\frac{\beta_A-\dfrac{g(1-r_B)}{1+g-r_A-r_Bg}}{\beta_A^0-\dfrac{g(1-r_B)}{1+g-r_A-r_Bg}}\right\}^{\frac{1-r_Ar_B}{(1-r_B)(r_A-1)}} \quad (6)$$

($\beta_A^0 = \beta_A$ when $\Psi = 0$) will be used to plot composition distribution curves. When $g = 1$, Eqn. (6) passes into Meyer and Lowry's formula[62] for molar composition distribution functions. The instantaneous composition of the macromolecules α_A is connected with the composition of the initial monomer mixture by the relation

$$\alpha_A=\frac{\beta_A^2(r_A-g)+\beta_Ag}{\beta_A^2(r_Bg+r_A-1-g)+\beta_A(1+g-2r_Bg)+r_Bg}. \quad (7)$$

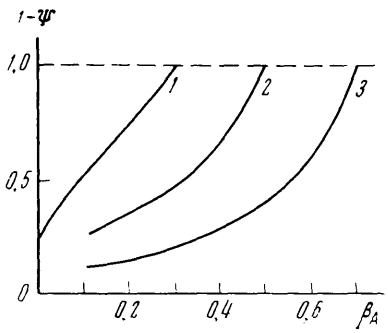


Figure 7. Monomer consumption curves for a model having $r_A = 3$, $r_B = 0.2$, and $g = 1.5$ with different values of β_A^0: 1) 0.3; 2) 0.5; 3) 0.7.[60]

Assuming now for concreteness $r_A = 3.0$, $r_B = 0.2$, and $g = 1.5$,[60] we plot the dependence of $1 - \Psi$ on β_A for several values of β_A^0 (Fig. 7). The integral composition distribution curve can easily be obtained from the composition diagram or by calculating α_A by means of Eqn. (7). (We again emphasise that the formalism involved in reproducing the integral curve takes into account only that "part" of the heterogeneity of composition which is unconnected with the fine structure of the chains.) From the integral curves for various values of β_A^0 it is easy to pass to the superposed integral curves for the heterophase process.

Fig. 8 shows integral composition distribution curves for models *1* and *2*. The substantial difference in corresponding curves is immediately apparent. In conformity with the second of the starting principles of this Section, however, we would like to lay special stress on the negligible difference between these models in the mean composition of the copolymers produced even despite the difference in form of the integral curves—unimodal distribution for the homophase process (curve *1*), and bi- and termodal distributions for the heterophase process (curves *2* and *3*)—and in the degree of heterogeneity of composition.

This is illustrated by Table 2, in which the parameter

$$f=(\bar{\alpha}_z-\bar{\alpha}_w)\bar{\alpha}_w=\left(\frac{\sum_{i=1}^{k}\alpha_i^2w_i}{k}-\sum_{i=1}^{k}\alpha_iw_i\right)\sum_{i=1}^{k}\alpha_iw_i \quad (8)$$

(k is the number of fractions, w_i is the proportion by weight of the ith fraction, and α_i is its weight-average composition) is a statistical measure of the heterogeneity of composition[63].

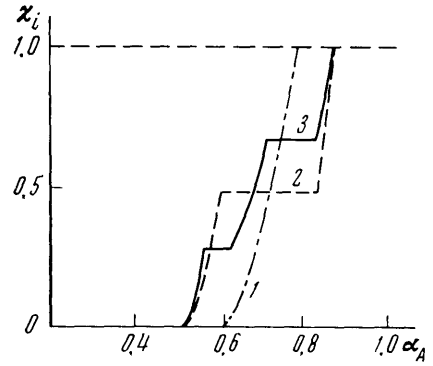


Figure 8. Integral composition distribution curves for copolymerisation: 1) homophase with $\beta_A^0 = 0.5$; 2) heterophase with $\Psi_{cr} = 0$ and $\Psi_I = \Psi_{II} = 0.25$; 3) heterophase with $\Psi_{cr} = 0.2$ and $\Psi_I = \Psi_{II} = 0.15$.

Comparison of the integral curves (Fig. 8) with the data in Table 2 leads to the conclusion[60] that use of the weight-average parameter $(\overline{\alpha_A})_w$ to describe the laws of heterophase copolymerisation may in individual cases produce gross errors. In other words, it is still more inappropriate to examine the heterophase process by means of the formalism developed to describe homophase copolymerisation than formally to process kinetic and statistical data for heterophase polymerisation by means of laws and equations for homophase polymerisation[8].

Table 2. Values of parameter f for certain models of copolymerisation ($r_A = 3$, $r_B = 0.2$, $g = 1.5$, $\Psi = 0.5$).

Process	Wt.-average composition of copolymer α_A	$10^3 f$	Process	Wt.-average composition of copolymer α_A	$10^3 f$
Homophase	0.71	2.4	Homophase for $0 \leqslant \Psi \leqslant 0.2$		
Heterophase $\Psi_{cr} = 0$ $\Psi_I = \Psi_{II} = 0.25$	0.70	19.4	Heterophase $0.2 < \Psi \leqslant 0.5$ $\Psi_I = \Psi_{II} = 0.15$	0.69	13.7

We can illustrate this by analysing the composition diagrams for homogeneous and heterogeneous copolymerisation (Fig. 9). In the heterophase process the position of a point on the composition diagram clearly depends not only on the substrate composition β_A^0 and the initial values of r_A and r_B but also on how and when (Ψ_c) the system separated into phases and on the ratio of the gross rates in each phase V^I/V^{II}. Thus the composition diagram itself is already arbitrary in character. In the simplest

two-phase systems the relation between β_A^I, β_A^{II}, and β_A can be described by the Langmuir adsorption law (see end of Section III).

The need for special caution in interpreting data on composition, kinetics, and molecular-weight distribution for heterophase systems is indicated also be results[64] (Fig. 10) for the effect of additions of zinc chloride complexing agents on the heterophase copolymerisation of acrylonitrile with vinylidene chloride, allyl alcohol, and vinyl acetate. This work is also interesting in that the experimental composition data are formally consistent with the Mayo—Lewis scheme (which applied also to individual points in Fig. 9). The insensitivity to phase separation of the canonical scheme of treating data is further evidence of the limited character of this scheme.

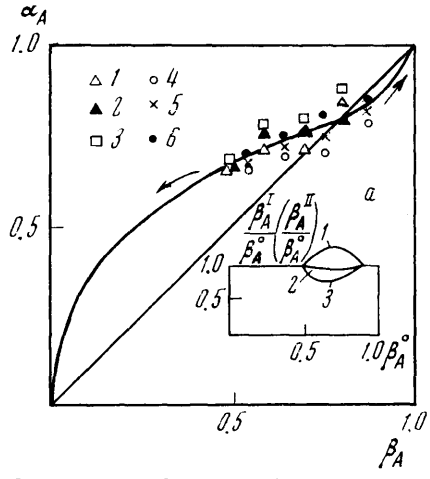


Figure 9. Composition diagrams for homophase (full curve) and heterophase (*a*) models of copolymerisation with $r_A = 0.1$, $r_B = 0.7$, $g = 0.8$, and $\Psi \leq 0.02$: models 1 and 2 with different ratios $(V^I/V^{II})_{\Psi \to 0}$: 1) 0.2; 2) 1.0; 3) 5.0; 4)—6) models 1—3 with the same ratios respectively [sic].

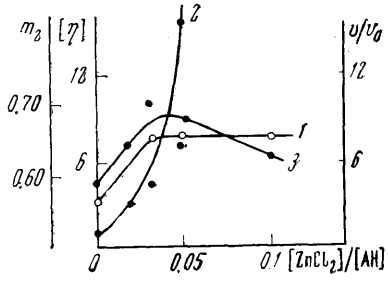


Figure 10. Effect of zinc chloride on heterophase process at 55°C: 1) composition m_2 of copolymer obtained from equimolecular mixture of vinylidene chloride and acrylonitrile (AH); 2) initial rate of copolymerisation; 3) intrinsic viscosity in dimethylformamide[64].

Heterophase copolymerisation is especially interesting at an azeotropic point ($\alpha'_A = \beta'_A$, $r_A < 1$, $r_B < 1$). For a classic homogeneous process the parameter $f = 0$ for $0 \leq \Psi \leq 1$ at an azeotropic point, but in a heterophase process the parameter $f \neq 0$ and should increase with Ψ even when both r_A and r_B are constant. In this case the very shape of the integral composition distribution curve should be unusual, with one branch convex and the other concave. Unfortunately, no work has yet been done which would enable these arguments to be tested.

Finally we note that heterophase copolymerisation would not exhibit a one-to-one correspondence between the individual integral curves, as occurs in classical cases of homophase copolymerisation[65]. This can be seen simply by comparing the composition distribution curves for homophase and heterophase copolymerisation[60].

V. ASPECTS OF THE KINETICS OF HETEROPHASE COPOLYMERISATION

The rates of consumption of monomers A and B in copolymerisations conforming to the complete Mayo—Lewis scheme are given by

$$\left.\begin{aligned} -\frac{dm_A}{dt} &= \frac{I^{1/2}}{\lambda}(r_A m_A^2 + m_A m_B) \\ -\frac{dm_B}{dt} &= \frac{I^{1/2}}{\lambda}(r_B m_B^2 + m_A m_B) \\ -\frac{d(m_A + m_B)}{dt} &= \frac{I^{1/2}}{\lambda}(r_A m_A^2 + 2m_A m_B + r_B m_B^2) \end{aligned}\right\}, \quad (9)$$

$$\lambda = (r_A^2 \delta_A^2 m_A^2 + 2\varphi r_A r_B \delta_A \delta_B m_A m_B + r_B^2 \delta_B^2 m_B^2)^{1/2}, \quad (10)$$

$$\delta_A = \frac{k_{tAA}^{1/2}}{k_{pAA}}; \quad \delta_B = \frac{k_{tBB}^{1/2}}{k_{pBB}}; \quad \varphi = \frac{k_{tAB}}{(k_{tAA} k_{tBB})^{1/2}}.$$

The rate constants for chain growth and termination are defined in terms of the reactions

$$\sim\!\dot{A} + \sim\!\dot{A} - (k_{tAA}) \to P; \quad \sim\!\dot{B} + \dot{B}\sim - (k_{tBB}) \to P;$$

$$\sim\!\dot{A} + \sim\!\dot{B} - (k_{tAB}) \to P; \quad \sim\!\dot{A} + A - (k_{pAA}) \to \sim\!A\dot{A};$$

$$\sim\!\dot{A} + B - (k_{pAB}) \to \sim\!A\dot{B}; \quad \sim\!\dot{B} + A - (k_{pBA}) \to \sim\!B\dot{A};$$

$$\sim\!\dot{B} + B - (k_{pBB}) \to \sim\!B\dot{B},$$

where P denotes a macromolecule. It is immediately apparent from formulae (9)—(10) that knowledge of the parameter λ—and hence also of δ_A, δ_B, and φ—is necessary in order to find the absolute reaction velocities dm_A/dt, dm_B/dt, and $d(m_A + m_B)/dt$. Great difficulty attends the experimental determination of all these quantities[7,8]. Furthermore, it has been shown for several systems that the parameters δ_A, δ_B, and φ themselves—and thus also λ—do not remain constant but are functions of β and Ψ.[66] The latter aspect greatly hinders the processing of kinetic data on random copolymerisation[67].

These difficulties can in considerable measure be eliminated by changing to relative parameters $dM_A/(dM_A + dM_B)$ or $dC_A/(dC_A + dC_B) = \alpha_A$. In fact α_A can be found by separate determination of the rates of consumption of the monomers A and B, while the degree of conversion

$$[(C_A)_{t=0} + (C_B)_{t=0} - (C_A)_t - (C_B)_t]/[(C_A)_{t=0} + (C_B)_{t=0}] = \Psi_t$$

is determined from the kinetic curves without special difficulty. (We recall that all calculations and arguments relate to quasi-stationary processes, when the lifetime τ of the macroradical is far shorter than the time $t_{\Delta\Psi_i}$ during which an increment of polymerisation $\Delta\Psi_i$ is produced[8].) In most real systems the condition $\tau \ll t_{\Delta\Psi_i}$ is satisfied automatically even for very rapid processes[7,67].

Taking this into consideration, we suggested[68,69] bypassing the difficulties of determining absolute rates of polymerisation of monomers A and B by analysing composition distribution curves. This is all the more useful in that the integral curves are themselves most important statistical characteristics of a copolymerisation. Replacement of kinetic by statistical analysis is only possible, of course, in those systems in which the consumption of each monomer can be followed separately.

We shall examine the kinetics of heterophase copolymerisation with such systems as example, and assume that model *2* in Section IV is valid. Unfortunately, no reliable experimental data are available, even for the primitive models *1* and *2*, which would enable specific numerical calculations to be made, so that our discussion must be most general in form. We shall suppose as before that at $\Psi \geqslant \Psi_c$ the consumption of the monomers can be determined separately in both phases. It can then readily be shown that the composition distribution function will be termodal for model *2* and bimodal for model *1*. In fact we use Eqns. (9) to describe the model, and choose the time t_q such that

$$\int_0^{t_q} \frac{I^{1/2}\{r_A[A]^2 + 2[A][B] + r_B[B]^2\}}{\lambda}\,dt = \frac{\{[A]+[B]\}_{t=0} - \{[A]+[B]\}_{t=t_q}}{\{[A]+[B]\}_{t=0}} \leqslant \Psi_c .$$

For $\Psi \leqslant \Psi_c$ we then have

$$-\frac{dA}{dt} = \frac{I^{1/2}\{r_A[A]^2 + [A][B]\}}{\lambda}; \quad -\frac{dB}{dt} = \frac{I^{1/2}\{r_B[B]^2 + [A][B]\}}{\lambda}, \quad (11a)$$

and for $\Psi > \Psi_c$, with copolymerisation occurring independently in phases I and II,

$$-\frac{dA^I}{dt} = \frac{(I^I)^{1/2}}{\lambda^I}\{r_A[A^I]^2 + [A^I][B^I]\}\ ,$$

$$-\frac{dB^I}{dt} = \frac{(I^I)^{1/2}}{\lambda^I}\{r_B[B^I]^2 + [A^I][B^I]\}\ , \quad (11b)$$

$$-\frac{dA^{II}}{dt} = \frac{(I^{II})^{1/2}}{\lambda^{II}}\{r_A[A^{II}]^2 + [A^{II}][B^{II}]\}\ ,$$

$$-\frac{dB^{II}}{dt} = \frac{(I^{II})^{1/2}}{\lambda^{II}}\{r_B[B^{II}]^2 + [A^{II}][B^{II}]\}\ , \quad (11c)$$

and in general $\lambda^I \neq \lambda^{II}$, as was shown experimentally for several systems[67]. If Ψ_c and v_k^I/v_k^{II} are known, and the above conditions (independent of the reactions in the two phases) are satisfied, formulae (11) can be used to obtain the integral composition distribution curves while omitting determination of the difficultly calculable λ, λ^I, λ^{II}, I^I, and I^{II}.

It can reasonably be expected that in real systems the shape of the integral curves will be influenced, in both models *1* and *2*, by monomeric mass exchange between the phases. This may lead to some smoothing of the integral curves. On the other hand, comparison of the integral curves at the same substrate composition but with different values of V, S, V_c, and v^I/v^{II} can give important information on the character of the mass exchange of monomers A and B and also on the properties of the interface. Unfortunately, no reports have been published of the simultaneous determination of rates of consumption of monomers in two phases, simply owing to the experimental difficulties. Furthermore, while the need for such investigations is obvious, little controlled work has been done in this field.

Data are usually available on the total rates of consumption of the monomers, i.e. $d(A^I + A^{II})/dt$ and $d(B^I + B^{II})/dt$. In this case even the change from rate curves to integral composition distribution curves becomes in some measure arbitrary[70,71]. If the volumes of phases I and II are comparable, and the overall rates of copolymerisation do not differ too greatly (roughly $0.2 < V^I/V^{II} < 5$), the integral curves obtained by processing the kinetic curves (for consumption of the monomers) are smoother than the real curves[72]. The main reason is that the instantaneous heterogeneity of composition depends considerably on the ratios

$$\left(\frac{dA^I}{dA^I + dB^I}\right)_{t=t_a}, \qquad \left(\frac{dA^{II}}{dA^{II} + dB^{II}}\right)_{t=t_a},$$

(or the corresponding ratios for the concentrations by weight of the monomers in the two phases, C_A and C_B). This alone suggests that the integral curves obtained from the consumption curves will underestimate the compositional heterogeneity. However, if the difference in the total rates of copolymerisation in the two phases is so large that we can reckon $V^I/V^{II} \gg 1$ or $V^I/V^{II} \ll 1$, good agreement must be expected between the real integral curves and those obtained from the consumption curves.

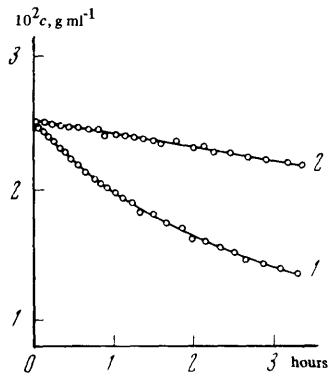


Figure 11. Rate curves for copolymerisation in dioxan with [I] = 0.2 wt.% at 70°C: 1) acrylamide; 2) maleic acid.

Nevertheless, even in the unfavourable range $0.2 < V^I/V^{II} < 5$ the consumption curves—$d(C_A^I + C_A^{II})/dt$ and $d(C_B^I + C_B^{II})dt$—show "anomalies" in heterophase copolymerisation (though not completely, in view of the above). "Anomalies" of this type were recorded[70] for the acrylamide—maleic acid system when the rate curves for copolymerisation in dioxan were analysed (Figs. 11 and 12). The integral curves obtained in this way cannot be defined[70,72] by two fixed copolymerisation constants in the range $1.0 \leqslant r_A < 3.0$ and $0 \leqslant r_B \leqslant 0.2$, which is additional evidence of the "special"[31] character of the copolymerisation of this system. Unfortunately, it was not possible in this work to estimate the time variation in the phase volumes and the overall reaction velocities in them, which limited the "degree of quantitativity" in the assessment of the "anomaly" and the contribution of the two-phase character of the system to it.

Work in which the "phasicity" was changed by varying the composition of a binary solvent is of interest in connection with overcoming (or bypassing) such difficulties. If copolymerisation is a homophase process at certain ratios χ of the components, but a heterophase process at others (beginning with a certain value χ_c), it can reasonably be expected that suitable control of the process variables in the vicinity of χ_c will enable us to judge the effect of adjustable parameters of the heterophase character on the appearance and the development of the "anomaly" in the integral curves. However, even here agreement can be obtained only in single researches.

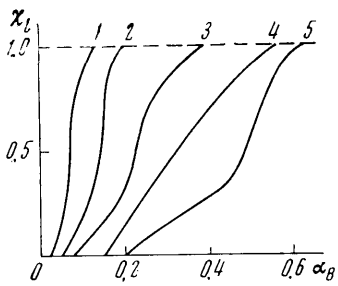


Figure 12. Integral composition distribution curves for copolymers of acrylamide (A) and maleic acid (B) in dioxan for different values of β_A (and Ψ_A): 1) 9 (0.69); 2) 4 (0.37); 3) 1 (0.39); 4) 0.67 (0.37); 5) 0.43 (0.34).

Thus studies[73,74] of the copolymerisation of 5% solutions of acrylamide with maleic acid in aqueous dioxan showed a variation in the relative reactivities of the monomers with change in the composition of the solvent mixtures and the same substrate composition, but apart from this the integral curves, after reaching χ_c, become more diffuse than those for homophase copolymerisation. The appearance of an "anomaly" originating from the heterophase character of the copolymerisation was illustrated[73,74] by analysing the position and shape of the integral curves for the same substrate composition but different values of χ. The parameters f for homophase and heterophase copolymerisation were also compared.

Kinetic anomalies were observed also on passing from a homophase to a heterophase process in work already referred to[55] (we recall that the "phasicity" of the process was determined here by the composition of the substrate). The overall kinetics of copolymerisation was determined dilatometrically, i.e. simultaneously in the two phases. Inversion of the rate was recorded for different substrate compositions (Fig. 13). With all the drawbacks of dilatometry applied to the investigation of multiphase processes, the results are nevertheless extremely significant. As was to be expected, the transition from homophase to heterophase copolymerisation is accompanied by "anomalous" kinetic relations. Similar conclusions can be reached from a careful examination of data in Ref. 75, also obtained in a dilatometric investigation of the copolymerisation of acrylonitrile with styrene.

An unusual form of kinetics was obtained for different substrate compositions (Fig. 14) in work already cited[53,54] on the copolymerisation of acrylonitrile (A) with sodium styrenesulphonate (B) in aqueous medium and in dimethyl sulphoxide. The most probable reason was the occurrence of a heterophase process in aqueous medium at substrate compositions [A] $\gg$ [B] and in dimethyl sulphoxide at [B] ≥ 10[A].

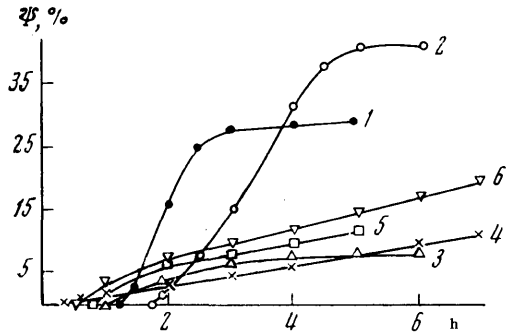


Figure 13. Kinetics of the copolymerisation of butadiene in mixtures with different initial contents (mole %) of phenyldichlorophosphine: 1) 5; 2) 10; 3) 20; 4) 30; 5) 40; 6) 50.

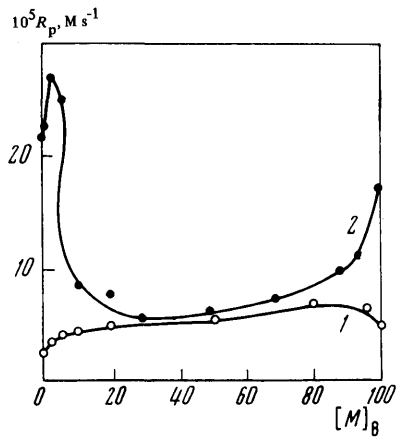


Figure 14. Dependence of initial rate of copolymerisation on composition of initial mixture of acrylonitrile (A) and sodium styrenesulphonate (B) in: 1) dimethyl sulphoxide; 2) aqueous medium at pH 7.

Kabankin et al.[76], in a kinetic investigation of the heterogeneous gas-phase copolymerisation of tetrafluoroethylene with ethylene and hexafluoropropene, were able to monitor the consumption of each monomer during the reaction by a previously developed technique[77,78]. The copolymerisation of ethylene with tetrafluoroethylene was studied also in a solvent, perfluorotriethylamine, when a heterophase process occurred. These workers emphasise that their values of r_A^* and r_B^* are arbitrary, since the true compositions of the initial mixture of monomers would differ from the mean values found from the composition of

the gaseous mixture at certain degrees of conversion. Figs. 15 and 16 illustrate the most typical results of this work. With certain reservations these workers conclude that the Mayo—Lewis scheme can be used to a first approximation for describing the heterogeneous and heterophase copolymerisations examined. In our opinion, however, Fig. 16 indicates rather the converse, i.e. that the "classical" or "canonical" scheme is not applicable to these systems.

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We are very far from intending to acknowledge any kind of "blind alley" in the theory of copolymerisation, but nevertheless must remark that the complexity of the determination of heterogeneity—especially of the separate determination of heterogeneity of composition itself and of differences in fine structure—greatly retards the development of theoretical work and to some extent engenders a tendency for calculations to be so approximate that *chemical* features of the process are neglected. With the limited number of examples available to us we have attempted to show that, even when the fundamental postulate (the ratio of reactivities—actually the copolymerisation constants) is satisfied, the Mayo—Lewis scheme may not work for thermodynamic and hence topochemical reasons.

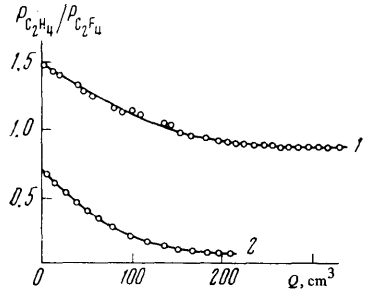


Figure 15. Dependence of relative partial pressures of ethylene and tetrafluoroethylene over perfluorotriethylamine solution on the consumption Q.[76]

On the other hand, both the previous[31] and the present reviews have shown the existence of entirely practicable and quite simple methods for converting "special" copolymerisation into the usual process or for controlling its "phasicity". The problem thus reduces to developing rational methods for analysing compositional heterogeneity and the fine structure. In this respect the position has improved in comparison with that reported previously[31]. For the first time compositional heterogeneity has been determined by rapid sedimentation with the use of two optical systems[79]. Inagaki[80] and Belen'kii et al.[81] have demonstrated quite convincingly the possibility of determining the *continuous* composition distribution function for copolymers by thin-layer chromatography. This method combined with gel chromatography and hydrodynamic experiments of the type described in Section IV may prove extremely sensitive also to the fine structure.

If the problem of the quantitative determination of heterogeneity of composition is solved—and there is every ground for hoping that this will occur in the near future—the statistical theory of copolymerisation may be expected to undergo the same improvements as occurred in the theory of homopolymerisation after reliable methods were developed for the analysis of molecular-weight distributions.

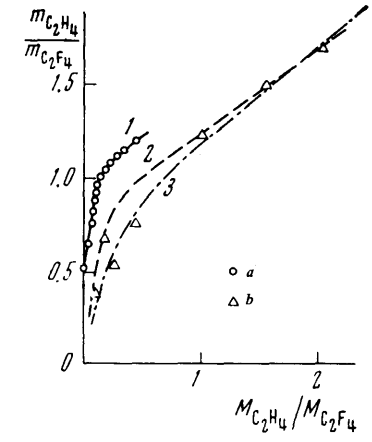


Figure 16. Composition diagrams for copolymers of ethylene and tetrafluoroethylene formed in: *a*) perfluorotriethylamine; *b*) gas phase. Theoretical composition curves for various values of $r_{C_2H_4}$ (and $r_{C_2F_4}$): 1) 0.61 (0.024); 2) 0.38 (0.10); 3) 0.46 (0.25).[76]

Certain polycondensation processes, especially interphase copolycondensation, are of interest in connection with "intervention" in the process and the simulation of copolymerisation. In this case problems of "phasicity" are solved relatively easily[82,83], and actual simulation can be achieved by suitable choice of difunctional reactants. Systems of this type are convenient also for the special investigation of processes developing in thin layers on one or other side of the interface[84].

Irrespective of how and when all these experimental problems will be solved, full responsibility can now be taken for stating that it is impossible to reach any quantitative conclusions from an analysis of the mean compositions of copolymers: this parameter is completely insensitive (cf. Table 2) to detailed kinetics and to any departures from the canonical scheme. Only analysis of heterogeneity of composition can give a complete idea of the mechanism of the process.

Consequently the attempts to reduce the reactivity of monomers to Alfrey—Price parameters determined from the equilibrium diagrams, still appearing in the literature, must be treated with great caution, and the use of copolymerisation as a *method* of analysing the activity of monomers in homopolymerisation must be approached with still greater caution and circumspection (the analysis of heterophase copolymerisation is, of course, implied).

At the same time we would like to direct the attention of investigators to interesting studies of the heterophase copolymerisation of styrene with acrylonitrile by Mino[85]

and with vinylidene cyanide by Gilbert, Miller, et al.[86] From an analysis of the composition distribution curves obtained by preparative fractionation the extremely significant conclusion was reached that copolymers obtained in a heterophase system show greater non-uniformity of composition than do those prepared under homogeneous conditions. The use of specially selected solvent–precipitant systems sensitive to the composition of the copolymer macromolecules[87,88] enables us to hope that information will be obtained on interphase interactions during synthesis. It would be especially interesting to isolate the copolymer separately from phases I and II, and to fractionate the two specimens. Such experiments are entirely practicable, at least for certain models of heterophase copolymerisation.

We would also like to emphasise that the conditions under which copolymerisation occurs need to be specified in works of reference, and in particular that it should be mandatory to indicate the "phasicity" of the process.

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Kazan Branch,
All-Union Scientific
Research Institute of
Synthetic Rubber

Institute of
Macromolecular
Compounds, USSR
Academy of Sciences

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Electrochemical Initiation of Polymerisation

G.S.Shapoval and A.V.Gorodyskii

Publications on the electrochemical initiation of polymerisation are surveyed, and methods are classified on the basis of the mechanism of the electrode reaction in which active centres are formed and the mechanism of growth of the polymer chain. The laws of the electrochemical initiation of radical and ionic polymerisation are analysed, and the advantages and prospects of the latter are shown. The features and possibilities of electrochemical initiation, leading to the formation of linear and network polymers, are examined on specific examples. A list of 138 references is included.

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I. INTRODUCTION

It was established long ago[1] that organic radicals could be formed during electrochemical oxidation or reduction. However, the use of such radicals to initiate polymerisation came only during recent years.

In 1939 Wilson[2] pointed out that reduction by alkali metals occurs in the same way as reduction at a cathode surface, and he suggested that electrochemical initiation of polymerisation was possible. Ten years later Dineen, Schwan, and Wilson[3,4] observed that, at a mercury cathode in acid medium, unsaturated compounds undergo hydrogenation with great difficulty, whereas they are rapidly polymerised. The advantages of such a process are obvious: the species responsible for initiating polymerisation are formed by an electrode reaction, so that the rate of initiation can be controlled very simply by varying the current density. It can be maintained constant or varied in pulses, which may yield a polymer having a narrow molecular-weight distribution.

Published information[5-8] indicates that electrochemical initiation may play a significant part in the solution of such important problems of polymer chemistry as the orientation of molecules during chain growth (stereoregulation), the creation of mild conditions of polymerisation, and the absence from the polymer of initiator fragments, which might in time cause degradation of the latter[9].

By no means all the potentialities of electrochemical initiation have been studied. Obviously for this reason it has not yet become so widespread as other, less controllable methods of initiation. However, the progress which has been achieved in replacing chemical initiation of the polymerisation of certain monomers, in particular halogenated alkenes[6,7], and the possibility of obtaining crystalline polymers during electrolysis[5,10], provide grounds for believing in the prospects for electrochemical initiation. This is perhaps the only electrochemical process in which considerably more than one mole of substance is transformed per faraday of electricity. The efficiency of the electrochemical reaction can be measured by the mean molecular weight of the resulting polymer.

A considerable number of publications have now appeared on the electrochemical initiation of polymerisation, but, apart from brief surveys mainly of the radical polymerisation of certain monomers[11-13], of dimerisation[14], and of a very narrow field[15], no papers of a review character have been published. Nevertheless, Breitenbach[16-18], Funt[19-23], Yamazaki[24], Parravano[25], and Soviet workers[26,27] have recently reported investigations of the electrochemical initiation of ionic polymerisation, in particular the preparation of "living" polymers[22-27]. Careful analysis of work on electrochemical initiation is urgently necessary in order to discuss the possibilities, merits, and defects of this method.

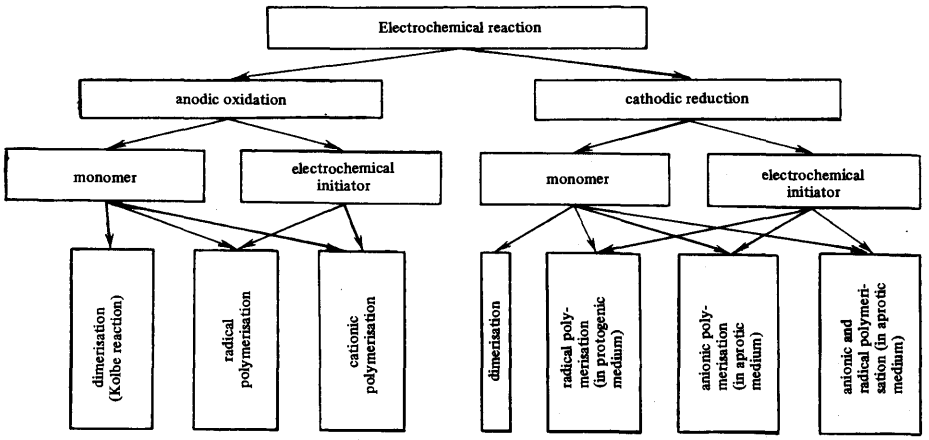
The polymer chain grows by a radical or an ionic mechanism depending on the conditions, and is little affected by whether initiation is electrochemical or chemical. The character of electrochemically initiated polymerisation is primarily determined by the mechanism and the rate of the electrode reaction. In the present Review, therefore, attention will be paid mainly to investigations of the mechanism and the kinetics of the electrode process and of the accompanying chemical reactions. From these data we can predict the yield of initiating species and of byproducts (resulting from dimerisation or complete reduction of the double bond), the accumulation of which prevents polymerisation.

II. CLASSIFICATION OF METHODS FOR THE ELECTROCHEMICAL INITIATION OF POLYMERISATION

Methods of electrochemical initiation can conveniently be classified according to the type of electrode process producing the initiating centres and according to the mechanism of growth of the polymer chain. Thus, depending on the type of electrode process, initiation is either anodic or cathodic; and according to the electrochemical reaction used initiation can occur either by (*a*) direct reduction or oxidation of the monomer or (*b*) oxidation or reduction of the electrochemical initiator, i.e. the compound whose anodic oxidation or cathodic reduction forms radicals or radical-ions capable of initiating polymerisation[10]. Radical and ionic (cationic or anionic) polymerisation processes are distinguished by the mechanism of chain growth. On the basis of this classification, Scheme I represents the types of electrochemical processes that have now been used for the initiation of polymerisation.

Thus the electrochemical reaction is usually a one-electron transition involving either the monomer or the electrochemical initiator. As a result active centres are formed on the electrode surface, and these are capable of

Scheme I



initiating either ionic or radical polymerisation depending on the conditions.

1. Anodic Oxidation

The direct electrochemical oxidation of organic compounds, in particular of carboxylate anions

$$C_nH_{2n+1}C(=O)O^- \rightarrow e \rightarrow C_nH_{2n+1}C(=O)O^{\cdot}\ , \qquad (1)$$

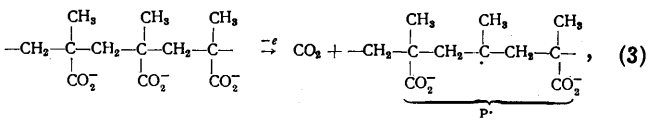
$$C_nH_{2n+1}C(=O)O^{\cdot} \rightarrow C_nH_{2n+1}^{\cdot} + CO_2\ , \qquad (2)$$

forms alkyl or alkanoxyl radicals, which then dimerise[1]. This is a particular case of electrochemical initiation—the Kolbe reaction, which has long served as a method for lengthening aliphatic hydrocarbon chains[28,29].

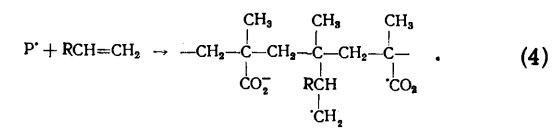
If the anodic oxidation of carboxylic acids or their salts is conducted in the presence of monomers, under appropriate conditions the radicals formed can initiate the radical polymerisation of such monomers as styrene, butadiene, isoprene, vinyl acetate, methyl methacrylate, and vinyl chloride[30-38]. Here the aliphatic acids and their salts undergoing oxidation at the anode are the electrochemical initiators.

Salts of metals of variable valency, in particular nickel(II) and manganese(II), can also be used as electrochemical initiators during anodic oxidation; Koval'chuk suggests[39,40] that during their electrolysis polymerisation is initiated by π-complexes with the monomer (e.g. acrylamide) of the metal in a higher valency state. Formation of such complexes is most probable on the adsorption at the electrode surface of a monomer whose double bond is polarised. Polymerisation can be initiated also by electrochemical oxidation of the sulphate anion, which may yield the radical-anion $SO_4^{\cdot-}$, capable of initiating polymerisation[41].

The use of macromolecular acids as electrochemical initiators is of undoubted interest. Thus the macroradicals of polymethacrylic acid obtained by anodic oxidation are able to interact with monomers[42]:



(3)



(4)

Such a reaction opens up great opportunities for modifying polymers[42,43].

In 1955 a method for the electrochemical initiation of the polymerisation of aliphatic halogenoalkenes was patented in Federal Germany[6,7].

The polymerisation of tri- and tetra-fluoroethylene initiated by peroxides takes place at high pressures (up to 100 atm) and temperatures (up to 100°C). Electrochemical initiation enables the process to be conducted at normal pressure and temperatures below 0°C. This eliminates the possibility of an explosive reaction, which at high temperatures may be caused by hot spots. Polymerisation is initiated by radicals formed at the anode during electrolysis, by $F^{\cdot}$ in hydrogen fluoride and by $CF_3^{\cdot}$ in trifluoroacetic acid. Low current densities enable the radicals to react with the monomer:

$$CF_3^{\cdot} + CF_2{=}CF_2 \rightarrow CF_3{-}CF_2{-}CF_2^{\cdot}\ . \qquad (5)$$

At low temperatures and high monomer concentrations chain growth can then occur with formation of a product of relatively high molecular weight[7].

If the radical formed by oxidation of the electrochemical initiator possesses high electron affinity, it may oxidise the monomer, which will lead to the initiation of cationic polymerisation[17].

2. Cathodic Reduction

A cathodic process results in formation of the initiating species both by direct reduction of the monomer and by reduction of the electrochemical initiator. The mechanism of growth of the polymer chain depends on the conditions. Thus direct electrochemical reduction of a monomer in a protogenic medium leads to formation of a radical (a protonated radical-anion) that initiates radical polymerisation[44-49], whereas in an aprotic medium anionic polymerisation takes place[5,17-22,50-53]†. Furthermore, simultaneous growth of the polymer chain by anionic and radical mechanisms is also possible during the early stages in an aprotic medium[8,20]. In several cases either an anionic or a mixed mechanism can be realised by conducting polymerisation in an aprotic medium and using cathodic reduction of an electrochemical initiator, in particular an alkali-metal ion[20].

The first electrochemical initiator of radical polymerisation to be used was the hydrogen ion[3,4,54,55], which on cathodic reduction causes the polymerisation of such monomers as methyl methacrylate, acrylic acid, vinyl acetate, etc.[56,57] According to the recombination theory of hydrogen overpotential[58] the efficiency of initiation depends on the electrode material and is a function of the overpotential[54]. Parravano[54,56] suggested that the initiating action of hydrogen atoms obtained electrolytically was analogous to their behaviour when adsorbed on a metal surface:

$$MH + R \rightarrow {}^{\cdot}RH + M \quad (6)$$

Mairanovskii[59] showed that a more probable mechanism in acid media is reduction of an already protonated monomer molecule, which as a result of the electrochemical process becomes the initiating agent[60,61]:

$$RH^+ + e \rightarrow {}^{\cdot}RH \quad (7)$$

This mechanism is supported by a phenomenon observed in the polarographic investigation of acrylamide[62]. This compound facilitates the electrochemical reduction of hydrogen, whose half-wave potential becomes more positive in the presence of this monomer, whereas that of acrylamide itself is independent of pH.[63] Thus, in the formation of a radical capable of initiating polymerisation, it is not the proton but the complex RH^+ that is reduced:

$$H^+ + R + e \rightarrow {}^{\cdot}RH \quad (8)$$

On the basis of views developed by Antropov[64] it can be concluded that the potential-determining stage is reaction (8), whose rate, according to the slow discharge theory[58], is given by

$$i = kC^S_{H^+}C^S_R \exp\left(-\frac{\alpha nFE}{RT}\right) \quad (9)$$

where i is the current, k is the rate constant of reaction (8), $C^S_{H^+}$ and C^S_R are the surface concentrations of protons and of acrylamide, α is the transfer coefficient of the electron (~ 0.5), F is Faraday's constant, and $n = 1$ is the number of electrons. Since the hydrogen diffusion current i_d remains unchanged in the presence of acrylamide, a definite concentration of the monomer, proportional to its concentration C_R in the solution, can be assumed to be present on the electrode surface:

$$C^S_R = k'C_R . \quad (10)$$

Then

$$E = E_0 + \frac{2RT}{F}\ln\frac{C_{H^+}}{i_d} + \frac{2RT}{F}\ln k'C_R - \frac{2RT}{F}\ln\frac{i}{i_d - i}, \quad (11)$$

whence

$$E = E_{1/2} + 0.118\lg\frac{i}{i_d - i}, \quad (12)$$

where

$$E_{1/2} = \text{const} + 0.118\lg C_R. \quad (13)$$

The experimental slope of this relation is close to the theoretical value (0.125 and 0.118 respectively).

The electrochemical reduction of oxygen can be used to initiate radical polymerisation[65]. Fedorova et al.[65] showed that the first stage involves the formation of hydrogen peroxide:

$$O_2 + e + H^+ \rightarrow HO_2^{\cdot}, \quad (14)$$

$$HO_2^{\cdot} + e + H^+ \rightarrow H_2O_2 . \quad (15)$$

This is then reduced to water:

$$H_2O_2 + e \rightarrow {}^{\cdot}OH + HO^-, \quad (16)$$

$$HO^- + H^+ \rightarrow H_2O, \quad (17)$$

$${}^{\cdot}OH + e + H^+ \rightarrow H_2O . \quad (18)$$

The radical $HO^{\cdot}$ formed as intermediate is able to initiate the polymerisation of methyl methacrylate and other derivatives of acrylic acid[66].

Radical polymerisation in aqueous medium can be initiated by a redox system in which the product of the cathodic reduction of one component reacts with the second component to form the initiating radicals[66]. An example is the cathodic reduction of tervalent iron in the presence of a peroxide:

$$Fe^{3+} + e \rightleftarrows Fe^{2+}, \quad (19)$$

$$Fe^{2+} + H_2O_2 \rightleftarrows Fe^{3+} + OH^- + {}^{\cdot}OH, \quad (20)$$

or

$$Fe^{2+} + S_2O_8^{2-} \rightleftarrows Fe^{3+} + SO_4^{2-} + SO_4^{\cdot-}, \quad (21)$$

The radical $HO^{\cdot}$ and the radical-ion $SO_4^{\cdot-}$ are able, as Kolthoff showed[66], to initiate the polymerisation of acrylic monomers:

$${}^{\cdot}OH + R \rightarrow HOR^{\cdot}, \quad (22)$$

$$SO_4^{\cdot-} + R \rightarrow {}^{-}SO_4 - R^{\cdot} . \quad (23)$$

Furthermore, a redox system can be established in which a cathode acts as reductant, while the oxidant is converted during reduction into an active polymerisation initiator[67,68]. The advantage of such a system in comparison with the preceding system is the possibility of controlling the rate of formation of initiating centres by eliminating intermediate stages.

Thus quite a wide range of reactions can now be used for the electrochemical initiation of polymerisation.

Since one of the main advantages of electrochemical initiation is the possibility of controlling the rate of polymerisation by varying the current density, we must

† The radical mechanism suggested originally[52,53] for the polymerisation of acrylonitrile in an aprotic medium with electrochemical initiation was subsequently revised. The absence of an inhibiting effect by diphenylpicrylhydrazyl and also experiments on the copolymerisation of acrylonitrile (study of the composition of the copolymers) established that polymerisation takes place by an ionic mechanism under these conditions[16,17].

examine in greater detail how this possibility is realised, starting not only from the mechanism of the electrode process but also from that of polymerisation as a whole.

III. RADICAL POLYMERISATION

1. Direct Electrochemical Reduction (Oxidation) of the Monomer

The simplest case of the electrochemical initiation of radical polymerisation in a protogenic solvent is direct cathodic reduction of the monomer. The first stage in this process is the actual electrochemical formation of the radicals capable of initiating polymerisation:

$$R + e + H^+ \underset{k_2}{\overset{k_1}{\rightleftarrows}} HR^{\cdot} . \qquad (24)$$

The rate of reaction (24) can be expressed[69] in terms of the current:

$$v = \gamma i = k_1 [R][H^+] \exp\left(-\frac{\alpha\varphi F}{RT}\right) - k_2 [{}^{\cdot}RH] \exp\frac{\beta\varphi F}{RT} , \qquad (25)$$

where φ is the electrode potential, α the transfer coefficient of the electron for the cathodic process, $\beta = 1 - \alpha$ the transfer coefficient for the anodic process, and γ (moles amp^{-1} cm^{-1} s^{-1}) a coefficient of proportionality. Formation of ·RH radicals is immediately followed by three parallel reactions, whose rates are limited by the rate of generation of these radicals—(i) recombination of the radicals on the electrode surface

$$ {}^{\cdot}RH + {}^{\cdot}RH \underset{k_4}{\overset{k_3}{\rightleftarrows}} HR{-}RH , \qquad (26)$$

at a rate

$$v_1 = k_3 [{}^{\cdot}RH]^2 - k_4 [H{-}R{-}R{-}H] ; \qquad (27)$$

(ii) further electrochemical reduction of ·RH at the same potential (an organic radical undergoes electrochemical reduction more readily than does the molecule from which it has been formed[70])

$$ {}^{\cdot}RH + e + H^+ \underset{k_6}{\overset{k_5}{\rightleftarrows}} RH_2 , \qquad (28)$$

at the rate

$$v_2 = \gamma i_2 = k_5 [{}^{\cdot}RH][H^+] \exp\left(\frac{-\alpha\varphi F}{RT}\right) - k_6 [RH_2] \exp\frac{\beta\varphi F}{RT} ; \qquad (29)$$

(iii) actual initiation of polymerisation—reaction of HR· with the monomer

$$HR^{\cdot} + R \underset{k_8}{\overset{k_7}{\rightleftarrows}} HR{-}R^{\cdot} , \qquad (30)$$

at the rate

$$v_3 = k_7 [{}^{\cdot}RH][R] - k_8 [{}^{\cdot}R{-}RH] . \qquad (31)$$

Since reactions (24), (26), (28), and (30) are irreversible[71,72], so that $k_2 = k_4 = k_6 = k_8 \to 0$, the second term on the right-hand side of Eqns. (25), (27), (29) and (31) can be neglected.

Thus, under otherwise similar conditions, both the actual rate of initiation and the yield of polymer depend on the rates of reactions (24) and (30), which in turn are determined by the electrode potential φ, the concentration of active centres HR·, and the concentration of the monomer R. However, increasing the rate of reaction (24) by raising the electrode potential (increasing the current density) leads to the accumulation of radicals HR· on the electrode surface, i.e. to an increase in the rates of reactions (26) and (28), which result in deactivation of the initiating species and hence decrease the rate of initiation and the polymer yield (after a certain time of electrolysis).

Radicals formed by cathodic reduction tend to be adsorbed, as a consequence of the presence of the unpaired electron[73]. The monomer can be assumed to react with the radical on the electrode surface, occupying unfilled sites on the latter. We express the surface concentration of radicals HR· in terms of the surface coverage θ, and that of the monomer [RS] in terms of its bulk concentration [R] and surface coverage:

$$[{}^{\cdot}RH] = f\theta , \qquad (32)$$

$$[R_S] = \varkappa [R](1-\theta) , \qquad (33)$$

where f and κ are proportionality coefficients. Equating to zero the second terms in Eqns. (25), (27), (29), and (31), and substituting for [·RH] and [RS], we obtain

$$v = k_1^* [R](1-\theta)[H^+] \exp\left(-\frac{\alpha\varphi F}{RT}\right) ,$$

$$v_1 = k_3^* \theta^2 , \qquad (35)$$

$$v_2 = k_5^* \theta [H^+] \exp\left(-\frac{\alpha\varphi F}{RT}\right) , \qquad (36)$$

$$v_3 = k_7^* \theta (1-\theta)[R] , \qquad (37)$$

where the k^* are rate constants allowing for f and κ.

The yield η of the polymer can be written provisionally as the ratio of the rate of reaction (30) to the sum of the rates of the parallel reactions (26), (28), and (30):

$$\eta = \frac{v_3}{v_1 + v_2 + v_3} . \qquad (38)$$

Then

$$\eta = \frac{k_7^* (\theta)(1-\theta)[R]}{k_3^* \theta^2 + k_5^* \theta [H^+] \exp\left(-\frac{\alpha\varphi F}{RT}\right) + k_7^* \theta (1-\theta)[R]} = \frac{k_7^* (1-\theta)[R]}{k_3^* \theta + k_5^* [H^+] \exp\left(-\frac{\alpha\varphi F}{RT}\right) + k_7^* (1-\theta)[R]} . \qquad (39)$$

Or, starting from formulae (25), (27), (29), and (31) with the assumptions adopted, we have

$$\eta = \frac{k_7 [{}^{\cdot}RH][R]}{k_3 [{}^{\cdot}RH]^2 + k_5 [{}^{\cdot}RH][H^+] \exp\left(-\frac{\alpha\varphi F}{RT}\right) + k_7 [{}^{\cdot}RH][R]} = \frac{k_7 [R]}{k_3 [{}^{\cdot}RH] + k_5 [H^+] \exp\left(-\frac{\alpha\varphi F}{RT}\right) + k_7 [R]} . \qquad (40)$$

Equations (39) and (40) show that the yield of polymer decreases with increase in electrode potential, the hydrogen-ion concentration, the free-radical concentration, and hence the surface coverage of the electrode. In fact the dependence of polymer yield on current density obtained by Funt[74] for the electrochemical initiation of the polymerisation of *N*-vinylpyrrolidone approaches zero asymptotically (Fig. 1). The dependence of polymer yield on monomer concentration established in this work (Fig. 2) also agrees well with Eqn. (40).

It is easy to show that, since the rate constant of the recombination of radicals k_3 is usually $\sim 10^7$–10^8 M^{-1} s^{-1},[72] the yield of polymer is insignificant even at low current densities. This is confirmed also by experimental results obtained by Dineen et al.,[3] Palit and Das[56], and Parravano[54] for the cathodic initiation of the polymerisation of various derivatives of acrylic acid, and also by Funt for the electrochemical initiation of the polymerisation of *N*-vinylpyrrolidone[74].

The radical polymerisation of acrylamide also proceeds similarly during its direct electrochemical reduction[45]. Two schemes were suggested to describe the mechanism, and explained satisfactorily the observed reactions of acrylamide (R). According to the first scheme (II) the interaction of two radical-anions leads to anionic polymerisation, which can develop only in an anhydrous medium. According to the second scheme (III) addition of a proton leads to formation of the radical HR$^{\cdot}$, which is capable either of initiating polymerisation or of recombining with formation of a dimer. Experiment showed[46] that the yield of polymer was negligible. Minute quantities (around 2–3 mg) of polyacrylamide were formed as a thin, water-insoluble film on the cathode surface.

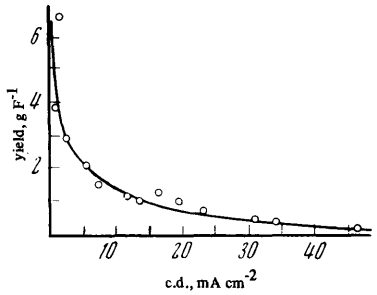


Figure 1. Effect of current density on current efficiency of polyvinylpyrrolidone formation[74].

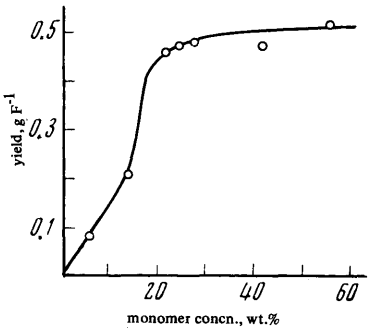


Figure 2. Dependence of yield of polyvinylpyrrolidone on monomer concentration with electrochemical initiation[74].

Another reason for such a low yield of polymer may be that the acrylamide dimers, trimers, or tetramers formed by recombination of the radicals or their interaction with the monomer diffuse slowly into the bulk of the solution, screening the electrode surface and thereby preventing transport of the monomer. Possible experimental support for this may be the unusually rapid fall in the cathodic peak for acrylamide when examined by oscillographic polarography at a stationary electrode with rapid polarisation by specified alternating current[63,75]. Yet the peaks representing reduction of simple ions under the same conditions do not vary with time[76]. Stable peaks for the reduction of acrylamide can be observed only with rapid rotation of the electrode[63].

The rate of initiation of radical polymerisation can be increased by rapid rotation of the electrode, which increases the rate of supply of monomer to its surface and somewhat diminishes coverage of the surface by $^{\cdot}$RH radicals. However, adsorption of radicals cannot thereby be completely eliminated or their recombination rate constant influenced. Because of adsorption of radicals, their recombination, and adsorption of the recombination products[59], the reaction is in effect localised on the electrode surface, and the most probable process is then formation of simple or additive dimerisation products, the yield of which was shown by Tomilov and Fioshin to be proportional to the current density[13,14].

	Scheme II	Scheme III
Electrochemical stage		$R+e \rightleftarrows R^{\cdot-}$
Chemical stage (*a*) in aqueous medium	$R^{\cdot-}+R^{\cdot-} \rightarrow {}^{-}R-R^{-}$	$R^{\cdot-}+H_2O \rightarrow HR^{\cdot}+OH^{-}$ $HR^{\cdot}+R \rightarrow HR-R^{\cdot}$ . . . . .
(*b*) in non-aqueous medium	${}^{-}R-R^{-}+2H_2O \rightarrow HR-RH+2OH^{-}$	$HR^{\cdot}+HR^{\cdot} \rightarrow HR-RH$
	${}^{-}R-R^{-}+nR \rightarrow {}^{-}R-(R)_n-R^{-}$	

Since the formation of initiating radicals occurs similarly during electrochemical oxidation and reduction, the above arguments apply both to the direct cathodic reduction and to the anodic oxidation of organic compounds, the radicals of which, as a consequence of the presence of the unpaired electron, tend to be adsorbed both on positively and on negatively charged surfaces[40]. High surface coverage and large recombination rate constants k_3 are the main conditions ensuring relatively high current efficiences for the formation of dimers[77], and this has served as a basis for their industrial production[13].

Thus one of the chief advantages of electrochemical initiation—the possibility of controlling the rate of the process by varying the current density—can be exploited, in radical polymerisation effected by direct reduction of the monomer, only over a narrow range of current densities at low surface coverage of the electrode.

2. Reduction (Oxidation) of the Electrochemical Initiator

If radicals are formed as a result of cathodic reduction or anodic oxidation of an electrochemical initiator, they are adsorbed on the electrode surface, as are the monomer radicals[40]. This is followed by preferential recombination either of the primary radicals or of products formed by them with the monomer. The probability of polymer formation is very small. This is confirmed by experimental results obtained by using the reduction of hydrogen[54–57] and oxygen[65] (hydrogen peroxide) in a protogenic medium for electrochemical initiation. The rate of initiation can be described, on certain assumptions, by equations analogous to those obtained for direct reduction of the monomer. As the processes are localised in a thin layer at the electrode surface, some increase in efficiency of initiation can be achieved by rapid rotation of the electrode and the use of very highly concentrated solutions of the monomer.

In order that initiation should be accomplished in the bulk of the solution, the species formed by the electrochemical reaction must be similarly charged to the electrode. This enables the charged species to leave the

electrode surface (the surface coverage to be reduced to a minimum). On the other hand, Coulombic repulsion prevents interaction between the charged species itself and lower polymerisation products. Chain growth—reaction between charged species and the monomer—predominates, which favours formation of a polymer of high molecular weight. In the choice of initiator satisfying these requirements it is necessary that the product of its electrochemical reaction should be able to initiate polymerisation of the chosen monomer under the given conditions.

3. Initiation of Polymerisation by Electrochemical Reduction of the Persulphate Ion

Persulphates are used to initiate polymerisation of vinyl monomers in water or in aqueous–organic emulsions. Their thermal decomposition produces $SO_4^{\cdot-}$ radical-anions, which are responsible for initiation[28,72,78,79]. According to Antropov[69] and Kryukova[80] this radical-anion is formed as intermediate also in the electrochemical reduction of the persulphate ion. On the basis of this hypothesis and the above requirements for an electrochemical initiator[81] potassium persulphate was used[67,68] for the electrochemical initiation of the polymerisation of acrylamide.

In this case initiation can be represented as consisting in (i) electrochemical reduction of the persulphate ion with formation of the radical-anion

$$S_2O_8^{2-} + e \underset{k_2}{\overset{k_1}{\rightleftarrows}} SO_4^{2-} + SO_4^{\cdot-} \qquad (41)$$

and (ii) chemical reaction between the radical-anion and the monomer

$$SO_4^{\cdot-} + R \underset{k_4}{\overset{k_3}{\rightleftarrows}} {}^{-}SO_4{-}R^{\cdot} . \qquad (42)$$

Since reactions (41) and (42) are almost irreversible[79,80], it can be assumed that $k_2 \ll k_1$ and $k_4 \ll k_3$. The rate of reaction (41) can then be written

$$v_1 = \gamma \cdot i_1 = k_1 [S_2O_8^{2-}] \exp\left(-\frac{\alpha\varphi F}{RT}\right) \qquad (43)$$

and the rate of reaction (42) as

$$v_2 = k_3 [SO_4^{\cdot-}] [R] . \qquad (44)$$

With a sufficiently high monomer concentration under steady-state conditions it can be postulated that

$$v_1 = v_2 = \text{const} \qquad (45)$$

i.e. the rate of initiation is equal to the rate of electrochemical formation of the radical-ions, and hence depends on the concentration of persulphate ions and the electrode potential. However, the rate of initiation can increase with rise in potential only until the latter permits further electrochemical reduction of the persulphate radical-ion

$$SO_4^{\cdot-} + e \underset{k_6}{\overset{k_5}{\rightleftarrows}} SO_4^{2-} . \qquad (46)$$

The rate of this process (allowing for the irreversible character of the reaction) is

$$v_3 = k_5 [SO_4^{\cdot-}] \exp\left(-\frac{\alpha_1\varphi F}{RT}\right) \qquad (47)$$

where α_1 is the transfer coefficient of the second electron.

Thus the rate of formation of the polymer, and hence its yield after a certain time of electrolysis, should be proportional to the electrode potential (current density) only until the latter reaches a certain value. Further rise in potential diminishes the yield.

The experimental dependence of the yield of polyacrylamide on the cathodic current density when potassium persulphate is used as electrochemical initiator in fact passes through a maximum at a certain current density (0.04 mA cm^{-2}). The shape of the curve is almost independent of the material of the electrode[45]. Fig. 3 shows that the rate of the electrochemical polymerisation of acrylamide can be controlled by varying the current density only in the range up to 0.04 mA cm^{-2}.

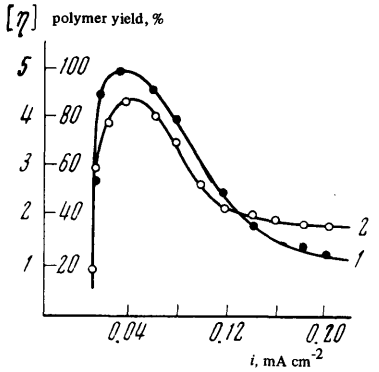


Figure 3. Effect of cathodic current density on formation of polyacrylamide: 1) yield; 2) intrinsic viscosity[45].

The dependence of the intrinsic viscosity of polyacrylamide on current density also shows a maximum. High values of the intrinsic viscosity may indicate a product of high molecular weight. The decrease in viscosity at a low current density is evidently an effect of dissolved oxygen, whose inhibiting action is apparent only at a low concentration of radicals, becoming insignificant when the concentration is considerable. One reason for the appearance of a descending section on the $[\eta]$–i curve at $i > 0.04$ mA cm^{-2} is the evolution of oxygen, which is able to interact with persulphate, acrylamide, and a growing polymer radical.

In the present case the yield of polyacrylamide at 0.03 mA cm^{-2} is proportional to the first power of the monomer concentration[45], in good agreement with Eqn. (44). A similar dependence of polymer yield on monomer concentration in solution was obtained by Funt in the electrochemical initiation of the polymerisation of vinylpyrrolidone[74] by its direct reduction (Fig. 2) (cf. also Eqn. 40).

With chemical initiation $SO_4^{\cdot-}$ radical-anions are formed not only in the thermal decomposition of persulphate ions[78] but also when the latter react with iron(II) compounds (reaction 21).[82,83] The persulphate ion then acts as oxidant in the redox process, which can be regarded as analogous to electrochemical reduction of the persulphate ion[84]. The rôle of reductant is played by the cathode, whose potential can be varied to shift the equilibrium in a required direction. When bivalent iron is used as reductant with the electrochemical initiation[66], an electrode process is necessary to maintain a certain concentration of reductant in the solution.

Thus the rate of initiation is determined by the rate of formation of active centres and the concentration of monomer with both direct and indirect (involving Fe^{2+} ions) electrochemical reduction of persulphate ions. Systems of the latter type have been successfully used by Kolthoff[66]. However, they are inferior to systems with direct electrochemical reduction of persulphate ions with respect to the possibility of controlling the rate of formation of initiating species[68].

IV. IONIC POLYMERISATION

Experience of the initiation of polymerisation by the electrochemical reduction of persulphate shows that formation of charged species by an electrode process considerably broadens the possibilities of electrochemical initiation, since it tends to spread the reaction into the bulk of the solution. However, this path provides only a partial solution of the problem of controlling the rate of the electrochemical initiation of polymerisation.

The most effective way of diminishing surface coverage of the electrode with active species is evidently to create in the polymerisable system conditions such that initiating anions would be generated on cathodic reduction, and cations by anodic oxidation, i.e. so that the initiation of ionic polymerisation would result from the electrochemical reaction. Systematic investigations in the field of ionic polymerisation have been made only during the past fifteen years[85-88], and the electrochemical initiation of such a process has been studied for barely ten years[19-25]. A few publications have appeared on the electrochemical initiation of ionic polymerisation[17-27,50-53], but the possibilities of the method and recent advances[5,23,24,26] suggest that such initiation is the most promising.

1. Cationic Polymerisation

Carbonium ions, capable of carrying the polymer chain, are formed as a result of the electrode reaction in the electrochemical initiation of cationic polymerisation[16-18]. They can be obtained by reaction of an oxidation product of the electrochemical initiator with the monomer[16] or by direct anodic oxidation of the latter[18]. Thus Breitenbach showed[16] that, when tetrabutylammonium or silver perchlorate is electrolysed in a monomer medium to which nitrobenzene has been added, polyacrylonitrile or poly-α-methylstyrene can be obtained in the anolyte by a cationic mechanism.

The suggested mechanism of initiation involves anodic oxidation of the perchlorate ion with formation of the radical $ClO_4^{\cdot}$

$$ClO_4^- \xrightarrow{k_1} ClO_4^{\cdot} + e \qquad (48)$$

and interaction between the radical and the monomer on the electrode surface to form a carbonium ion

$$ClO_4^{\cdot} + R \xrightarrow{k_2} ClO_4^- + R^+ \ . \qquad (49)$$

The carbonium ion, having like charge to the anode, passes into solution, carrying with it the polymer chain. Carbonium ions are formed similarly when the tetrafluoroborate anion is used as electrochemical initiator[53].

The rate of initiation due to oxidation of the electrochemical initiator is given by the equations

$$v_1 = k_1[ClO_4^-]\exp\frac{\beta\varphi F}{RT}\ , \qquad (50)$$

$$v_2 = k_2[ClO_4^{\cdot}][R]\ . \qquad (51)$$

In a steady state $v_1 = v_2$, and the overall rate of polymerisation is evidently determined by the rate v_1 of the electrode reaction, which varies exponentially with the electrode potential and very little with the concentration of perchlorate ions, which are regenerated by reaction (49). However, the rate of polymerisation depends strongly on the concentration of the monomer, which can be adsorbed on the electrode only until it reacts with the electrochemical initiator[40]. The cation, of like charge to the electrode, then diffuses into the bulk of the solution, where it initiates cationic polymerisation.

The second possible mode of electrochemical initiation of cationic polymerisation—direct anodic oxidation of the monomer

$$R \xrightarrow{k_1} R^+ + e \qquad (52)$$

was accomplished by Breitenbach with styrene, isobutyl vinyl ether, and *N*-vinylcarbazole[17,18].

Breitenbach compared the polarographic oxidation half-wave potentials $E_{\frac{1}{2}}$ for several monomers with the Q–e scheme of copolymerisation parameters‡.[18] The Table shows that the value of $E_{\frac{1}{2}}$ gives an idea of the mechanism of the formation of active centres during the electrochemical initiation of cationic polymerisation and copolymerisation, and also indicates the activity of monomers in this process.

Anodic oxidation potentials of some monomers in acetonitrile (rotating platinum electrode in tetraethylammonium perchlorate as supporting electrolyte; reference electrode Ag/AgCl in acetonitrile) and values of the parameter e in the Q–e scheme.

Depolariser	Oxidation potential $E_{\frac{1}{2}}$, V	e
N-Vinylcarbazole	1.14	—1.40
N-Vinylpyrrolidone	1.67	—1.14
Isobutyl vinyl ether	2.07—2.11	—1.77
Indene	1.73—1.76	—1.03
Phenylacetylene	2.12—2.30	—0.66
Styrene	1.99—2.05	—0.80
p-Methoxystyrene	1.45 1.60—1.80	—1.11
p-Methylstyrene	1.80—1.89	—0.98
p-Chlorostyrene	2.02—2.06	—0.33
α-Methylstyrene	2.00	—1.27
2-Vinylpyridine	2.72—2.80	—0.50
4-Vinylpyridine	—	—0.20
Acrylonitrile	—	+1.20
Methyl methacrylate	—	+0.40
Vinyl acetate	—	—0.22

The rate of initiation with direct oxidation of the monomer

$$v = k_1[R]\exp\frac{\beta\varphi F}{RT} \qquad (53)$$

depends on the monomer concentration and the electrode potential. An analogous relation should be observed for the yield of polymer after a certain period of electrolysis.

Although the possibility of the electrochemical initiation of cationic polymerisation has been demonstrated and

‡ Q and e are parameters in the Alfrey–Price equation, representing respectively the reactivity of the radical towards the monomer and the polarisation of the monomer molecule[89].

explained theoretically, it has been accomplished in only a few cases by Breitenbach and his coworkers[16,17,52,53] and also by Strobel and Schulz[90].

2. Anionic Polymerisation

The cathodic reduction of an electrochemical initiator in an aprotic medium—in the absence of electron-accepting impurities, in particular moisture and oxygen—followed by interaction with a monomer or the direct electrochemical reduction of the monomer to form a radical-anion leads to the initiation of anionic polymerisation[5,19-25]. Radical-anions, bearing a like charge to the cathode, are not adsorbed on its surface, but diffuse into the interior of the solution. They interact to form dianions; chain growth then takes place from the two ends by an anionic mechanism, as with chemical initiation[86,87].

(*a*) Initiation by reduction of electrochemical initiator

Electrochemically initiated polymerisation is usually accomplished in the presence of an electrically conducting additive (a tetra-alkylammonium or an alkali-metal salt). If the electron affinity of the metal ion of the additive is greater than that of the monomer, an amalgam of the metal may be obtained on the cathode during electrolysis, which will react with the monomer to form species capable of initiating anionic polymerisation:

$$M^+ + e \underset{k_2}{\overset{k_1}{\rightleftarrows}} M, \tag{54}$$

$$M + R \underset{k_4}{\overset{k_3}{\rightleftarrows}} M^+ + R^{\cdot-}, \tag{55}$$

$$R^{\cdot-} + R^{\cdot-} \xrightarrow{k_5} {}^-R{-}R^-, \tag{56}$$

$${}^-R{-}R^- + R \xrightarrow{k_6} {}^-R{-}R{-}R^-. \tag{57}$$

The rates of each stage in the process are

$$v_1 = k_1[M^+]\exp\left(-\frac{\alpha q F}{RT}\right) - k_2[M]\exp\frac{\beta q F}{RT}, \tag{58}$$

$$v_2 = k_3[M][R] - k_4[M^+][R^{\cdot-}], \tag{59}$$

$$v_3 = k_5[R^{\cdot-}]^2. \tag{60}$$

The rate of the electrode reaction depends on the cathode potential and very little on the concentration of the electrochemical initiator, since metal ions are regenerated by interaction with the monomer (reaction 55).

The efficiency of initiation, which may be measured by the constant k_3 of the forward reaction (55), is determined by the difference in electron affinity between the metal M and the monomer[86-88,91]. This quantity is constant for each metal–monomer pair. Thus as a result of the electrochemical reaction we arrive in effect at chemical initiation by an amalgam of the alkali metal. However, the electrode is always negatively charged, so that anions are repelled from its surface, whereas in chemical initiation the metal amalgam may acquire a positive charge during interaction with the monomer, which will tend to attract radical-anions[92].

Control of the rate of the process, with electrochemical reduction of the metal ion, is somewhat restricted by the fixed value of k_3. In order to increase this constant it is necessary to select a metal–monomer pair such that the metal possesses a low ionisation potential, while the monomer has a high electron affinity[88,91]. Nevertheless, if the electron affinity of the monomer exceeds that of the metal ion of the electrochemical initiator, radical-anions are formed by direct cathodic reduction of the monomer[20].

(*b*) Initiation by direct reduction of monomer

The electron affinity of various compounds (in particular aromatics) varies in parallel with the half-wave potential for their polarographic reduction[93]. Thus the mechanism of formation of the active centres responsible for initiation of anionic polymerisation can be assessed in each specific system from polarographic data. If the half-wave potential for the cation of the supporting electrolyte is more negative than the half-wave potential of the monomer, electrochemical initiation of polymerisation will occur by direct reduction of the monomer[21,23,24,94] to the radical-anion

$$R + e \underset{k_2}{\overset{k_1}{\rightleftarrows}} R^{\cdot-} \tag{61}$$

whose dimerisation yields a dianion carrying the polymer chain[85,95] (reactions 57 and 61). The rate of the electrochemical stage

$$v_1 = k_1[R]\exp\left(-\frac{\alpha\varphi F}{RT}\right) - k_2[R^{\cdot-}]\exp\frac{\beta\varphi F}{RT} \tag{62}$$

is proportional to the concentration of the monomer and depends on the electrode potential φ ($k_2 \to 0$). The rate of chemical reaction of the radical-anions (Eqn. 60) is limited by their rate of formation and by Coulombic repulsion. The rate of growth of the polymer chain (reaction 57)

$$v_2^* = k_6[{}^-R - R^-][R] \tag{63}$$

is determined by the concentration of initiating dianions and the monomer. The rate of formation of the polymer (its yield after a definite time)

$$\eta = f(v_2^*) = f(v_1 + v_3) \tag{64}$$

(v_3 from Eqn. 60) is directly dependent on the electrode potential (current density), as is observed in practice (Fig. 4).

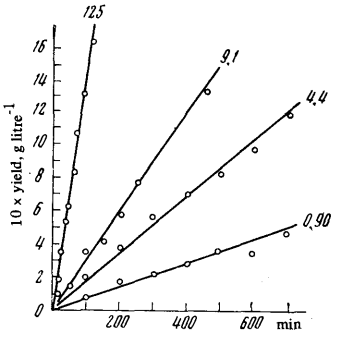


Figure 4. Dependence of yield of polyacrylonitrile on duration of reaction for various currents (mA).[21] The area of the electrode was the same (1 in^2) in all experiments.

Feoktistov and Tomilov[96,97], with acrylonitrile as example, showed that the dianion $R^=$ may be formed by direct two-electron reduction of the monomer. This mechanism is atypical of other monomers. Nevertheless, the rate of initiation and hence the yield of polymer are

determined even in this case by the electrode potential and the monomer concentration.

Thus there exist various types of electrode reactions, as a result of which either radical or ionic polymerisation occurs depending on the conditions. The above survey shows that one of the most attractive features of electrochemical initiation—the possibility of controlling the rate of polymer formation—can be successfully realised only in the initiation of ionic polymerisation. In the case of radical polymerisation ways must be sought of diminishing the surface coverage of the electrode by active species.

3. Possibilities of Simultaneous Radical and Ionic Mechanisms of Chain Growth with Electrochemical Initiation

A radical-anion formed by reaction (55) or (61) has an unpaired electron in the lowest vacant π-orbital[85] of the monomer. This electron is usually delocalised, so that the recombination of monomeric radical-anions (reaction 56) is, according to Szwarc[85,86] and to Bagdasar'yan[98], the slowest stage in the initiation of anionic polymerisation and limits the overall rate of polymerisation. Funt reaches a similar conclusion from an investigation of the electrochemical initiation of the anionic polymerisation of acrylonitrile[21].

At a sufficiently high monomer concentration (at the electrode surface) reactions (61) and

$$R^{\cdot-} + R \xrightarrow{k_5} {}^{\cdot}R{-}R^{-} \qquad (65)$$

can evidently occur consecutively. This involves stabilisation of anionic and radical ends, after which the dimeric radical-anions may undergo recombination

$${}^{\cdot}R{-}R^{-} + {}^{\cdot}R{-}R^{-} \xrightarrow{k_6} {}^{-}R{-}R{-}R{-}R^{-} \qquad (66)$$

and chain growth by an anionic mechanism; in the limiting case the chain may grow at the two ends simultaneously by radical and anionic mechanisms

$${}^{\cdot}R{-}R^{-} + R \xrightarrow{k_7} {}^{\cdot}R{-}R{-}R^{-}. \qquad (67)$$

The possibility of such a process was postulated by Tobolsky et al. in the polymerisation of styrene initiated by metallic sodium[99] and by Funt et al.[21] under conditions of electrochemical initiation. The latter workers discovered that the composition of a copolymer of acrylonitrile with methyl methacrylate or styrene indicates that a radical mechanism of polymerisation predominates at the start of electrolysis (polymerisation), and an anionic mechanism as time elapses.

The possibility of the simultaneous addition of monomer molecules to anionic and radical ends of a radical-ion has been confirmed by experiments on the inhibition of the electrochemically initiated polymerisation of acrylonitrile in dimethylformamide[8,95]. Such chain-transfer agents for radical polymerisation as benzene, toluene, and chlorobenzene, which can be adsorbed on the electrode[100], partly inhibit the cathodic polymerisation of acrylonitrile, diminishing the yield of polymer by ~ 20%, whereas they completely inhibit anodic polymerisation (a purely radical process).

It is difficult to determine the rate of reactions (65) and (66). Since, however, k_5 evidently exceeds k_6, and the rate of chain growth by anionic polymerisation at low temperatures and in the absence of impurities considerably exceeds the rate of growth by radical polymerisation, the total rate of polymerisation can be assumed to be determined by the electrode potential and the monomer concentration, as in anionic polymerisation.

4. Electrochemical Initiation of the Anionic Polymerisation of Isocyanates

The electrochemical initiation of anionic polymerisation can be most conveniently studied on monomers that cannot be polymerised by any other mechanism. A classic example of this is phenyl isocyanate, which can be polymerised only by an anionic mechanism[101-103]. The possibility of the electrochemical reduction of phenyl isocyanate has been shown polarographically[104]. On reduction at a dropping mercury electrode in dimethylformamide this compound gives a single polarographic wave representing the addition of two electrons by the reactions

$$R + e \rightarrow R^{\cdot-}, \qquad (68)$$

$$R^{\cdot-} \xrightarrow{PD} {}^{\cdot}RH, \qquad (69)$$

$${}^{\cdot}RH + e \rightarrow {}^{-}RH, \qquad (70)$$

$${}^{-}RH \xrightarrow{PD} RH_2, \qquad (71)$$

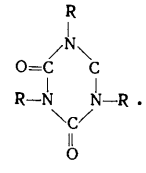
(where PD represents a proton donor).

This mechanism is possible at low concentrations of phenyl isocyanate, when sufficient hydrogen ions are present at the electrode surface to protonate the reduced molecule§. At considerable concentrations of the isocyanate ([R] ≫ [H_2O]) its wave divides into two. The second wave corresponds to addition of an electron to the radical-anion at a more negative potential:

$$R^{\cdot-} + e \rightarrow R^{=} \qquad (72)$$

With increase in the isocyanate concentration, however, the second wave does not grow but diminishes: the total height of the waves approaches the height of a one-electron wave, so that the number of added electrons n changes from 2 to ~ 1. The reason is that the radical-ions of phenyl isocyanate recombine to form a bianion (reaction 56), which is able to initiate polymerisation.

These results suggest that electrochemical initiation of the anionic polymerisation of phenyl isocyanate can occur at a monomer concentration of 0.02 M and an electrode potential (current density) corresponding to the potential of its first wave. Electrolysis of a solution of phenyl isocyanate in an aprotic medium in fact yields a polymer[5] corresponding in properties to the poly(phenyl isocyanate) obtained by the action of anionic catalysts[101,103]. The suggested mechanism of electrochemical initiation by direct reduction of the monomer with cleavage of the N=C bond is confirmed by the elementary composition and the infrared spectra of the resulting poly(phenyl isocyanate) and by the formation, under the same conditions at room temperature, of the trimer[105,106]



The yield of polymer increases with fall in temperature, increase in monomer concentration, and decrease in

§ Karl Fischer's method indicates that well dehydrated dimethylformamide contains 0.01% of moisture, corresponding to a concentration of ~ 0.005 M: i.e. the quantity of water is comparable with the concentration of depolariser.

current density[10,107], which agrees well with the general laws of anionic polymerisation with chemical initiation. The increase in polymer yield with decrease in current density observed in this work appears at first glance to be inconsistent with Eqn. (62) for the rate of electrochemical formation of the active centres responsible for the initiation of anionic polymerisation. The explanation is that at a high current density the rate of formation of the cyclic trimer of phenyl isocyanate by an anionic mechanism increases, which lowers the rate of initiation of actual polymerisation. Isocyanates are known to tend to form trimers[101,102].

Special stress must be laid on the crystallinity of the poly(phenyl isocyanate) obtained by electrochemical initiation: i.e. it has a regular structure, as indicated by the coincidence of its X-ray patterns with those of the polymer obtained by Natta[101] using stereospecific catalysts. With chemical initiation the crystallinity of the polymer is strongly dependent on the solvent, gegenion, and temperature[108]. With electrochemical initiation crystalline poly(phenyl isocyanate) was obtained in such solvents as dimethylformamide, oxolan, and acetone in the presence and in the absence of tetrabutylammonium iodide.

All this is evidence that, with electrochemical initiation, stereoregularity is largely achieved by orientation of monomer molecules on the electrode surface in the initial stages of growth of the polymer chain. Thus with phenyl isocyanate as example it has been shown for the first time that stereospecific polymerisation is fundamentally possible with electrochemical initiation.

5. Preparation of "Living" Polymers by Electrochemical Initiation

During the 1960s so called "living" polymers aroused the special interest of scientists in the field of anionic polymerisation. Such polymers were first obtained by Szwarc[91] by polymerising α-methylstyrene in a non-polar medium under the influence of metallic sodium or an alkali-metal alkyl[85,86]. Great advances in the field of anionic polymerisation were made by Soviet investigators—Medvedev's school[109-112], Bagdasar'yan[98], Erusalimskii[113,114], Enikolopyan[115,116], and Lipatova[117]. A "living" polymer is brightly coloured owing to the presence of the ion-pairs $\sim CH_2CHAr^-M^+$ at the ends of the macromolecules (M = Na, Li). Fresh portions of a monomer undergo polymerisation when added to a solution of a "living" polymer. Polymers obtained in this way have a narrow molecular-weight distribution.

Electrochemical initiation of polymerisation, as a result of which "living" polymers are obtained, allows either the number of active centres to be changed during polymerisation or their rate of formation to be maintained constant, in addition to the general opportunities available with chemical initiation.

Furthermore, increasing attention has been paid during recent years to polymers (oligomers) having definite functional terminal groups. They are usually obtained by adding to a solution of a "living" polymer compound which react with the "living" carbanion to form new functional groups at the ends of the macromolecule[91]. Thus the addition of proton donors results in the appearance of hydrogen at the ends of a polymer chain, carbon dioxide yields a carboxy-group, oxiran produces a hydroxyl, etc.

A virtue of electrochemical polymerisation is the possibility of deactivating "living" polymers by changing the polarity of the electrodes, i.e. the possibility of obtaining terminal groups of a polymer by interaction of the products of anodic and cathodic reactions[23]:

$$^-R—R_n—R^- + 2R_1^+ \rightarrow R_1—R_{n+2}—R_1 \quad (73)$$

This feature of electrochemical initiation opens up new routes for the synthesis of macromolecules having specified terminal groups.

Yet another important advantage is that electrochemical initiation enables "living" radical-anions to be obtained by direct cathodic reduction of the monomer, eliminating the stage of preparation of a catalyst, which is especially sensitive to contamination by moisture and oxygen[91].

(*a*) Preparation of linear "living" polymers

Especially clean conditions—absence of contamination and of impurities of proton-donating and electron-accepting character—are required to obtain "living" polymers by an anionic mechanism. Electrochemical "living" poly-α-methylstyrene was first obtained in 1965 by Yamazaki et al.,[24] who electrolysed a solution of the monomer in oxolan in the presence of lithium tetrahydroaluminate and a sodium tetra-alkylaluminate. This polymer had a bright cherry-red colour and a quite high molecular weight. Values found for the molecular weight were close to those calculated by means of the formula[23]

$$M_n = \frac{[M]}{0.5I} \quad (74)$$

(I is the number of faradays of electricity and [M] the concentration of the monomer), which was deduced on the assumption that polymerisation was initiated by dianions formed by recombination of radical-anions produced initially (i.e. it was assumed that two electrons were consumed in the formation of one macromolecule).

The bright colour of the styrene carbanions formed by electrolysis enables the rate of formation of active centres to be followed from the variation in the absorption maximum (λ_{max} = 340 nm) in the electronic spectrum, and their rate of disappearance from the change in polarisation of the electrodes.

The possibility of obtaining "living" polymers in liquid ammonia by the electrochemical initiation of anionic polymerisation is especially noteworthy. Thus Parravano et al.[25] electrolysed 4-vinylpyridine in liquid ammonia, and obtained in quantitative yield at the cathode a polymer of molecular weight $(6-10) \times 10^4$ and a quite narrow molecular-weight distribution (M_W/M_n = 1.5). In this case initiation takes place in the bulk of the solution, by addition of a so called "solvated" electron to the monomer, which involves formation of radical-anions and their recombination products—bianions. Current efficiencies of 0.5 mole F^{-1} are cited as evidence of the suggested mechanism.

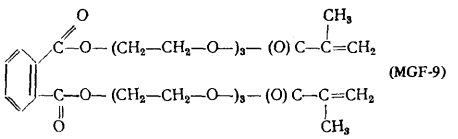
Experiments in which polymerisation occurred after addition of a second portion of the monomer, without further electrolysis, confirm that the polymer obtained is "living".

(*b*) Preparation of network "living" polymers

If a monomer contains two or more double bonds, a three-dimensional network polymer is formed, which under certain conditions may be "living". Lipatova and Siderko obtained such "living" network polymers by anionic polymerisation with chemical initiation from oligo(ether-acrylates).[117] These compounds contain reducible groups

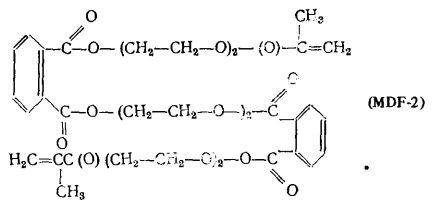
(phthalate and methyl methacrylate[118]) differing in electron affinity and separated by a system of σ-bonds. All this makes them interesting both with regard to the laws of anionic polymerisation itself and with regard to the mechanism of their electrochemical reduction and the formation, during the electrochemical reaction, of the active centres responsible for the initiation of polymerisation.

The possibility of obtaining "living" network polymers from oligo(ether–acrylates) by electrochemical initiation was established in the cases of bismethacryloyloxyethoxyethyl phthalate (MGF-9)



(MGF-9)

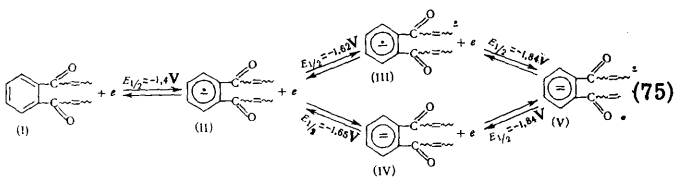
and oxadiethylene bis(methacryloyloxyethoxyethyl phthalate) (MDF-2)¶



(MDF-2)

It is especially noteworthy that a "living" polymer can be obtained by electrochemical initiation from an oligo(ether–acrylate) not only under a high vacuum (with oxolan as medium), as in the electrochemical polymerisation of styrene[23,24], but also in such a highly polar solvent as dimethylformamide (with addition of tetrabutylammonium iodide and a current of argon)[25,119,120].

Investigation of the mechanism of the electrochemical reduction of oligo(ether–acrylates) by polarography and oscillographic polarography with a specified alternating current and the use of model compounds (methyl methacrylate and dimethyl phthalate) shows that the transfer of electrons to the oligomer molecule is a stepwise process, characterised by three diffusion waves[121], and each electrochemically active group is reduced independently of the others[27]. From the half-wave potentials of the functional groups in the oligomer the electrochemical reduction of MGF-9 can thus be represented[27]



(75)

Products (III) and (V) are able to initiate anionic polymerisation, whereas the products of the one- and two-electron reduction of the phthalate group in the oligomer (II and IV respectively) do not cause polymerisation, although the solution on electrolysis has the bright colour characteristic of the radical-ion or the dianion of dimethyl phthalate.

Thus the electrochemically reduced oligo(ether–acrylate) molecules carry 1–3 negative charges. On the one hand this causes repulsion from the cathode of similarly charged species, i.e. the occurrence of polymerisation in the bulk of the solution; on the other hand, it promotes formation of a polymer network from previously uncoiled oligomeric blocks, which in turn produces a certain (fibrillar) supermolecular structure in the polymer, as is confirmed by electron microscopy[122].

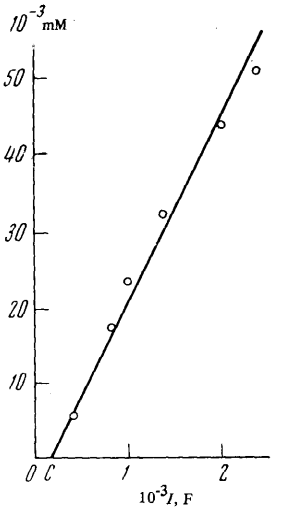


Figure 5. Dependence of yield of network poly(ether–acrylate) on quantity of electricity that has passed through 0.5 M solution of MGF-9 oligo(ether–acrylate) in dimethylformamide[120].

Features of the mechanism of the electrochemical initiation of polymerisation associated with the specific structure of oligo(ether–acrylates) affect the dependence of polymer yield on the quantity of electricity that has passed through the oligomer solution. According to Eqn. (64) the yield of polymer with electrochemical initiation of anionic polymerisation is proportional to the monomer concentration and to the quantity of initiating particles formed by the electrode reaction (to the electrode potential). In the present case the yield is actually proportional to the concentration of oligo(ether–acrylate). Nevertheless, the dependence of the yield of poly(ether–acrylate) on the quantity of electricity that has flowed through the solution is a straight line not passing through the origin (Fig. 5). The reason is that part of the electricity is consumed in charging the oligomer molecules (formation of products II and IV in reaction 75), which confirms the suggested scheme of electrochemical reduction of these compounds. The straight line is represented by the equation

$$\eta = K(I - I_{thr}), \qquad (76)$$

where η (expressed as molarity of oligomer that has reacted) is the yield of polymer, I (F) the quantity of electricity that has passed through during electrolysis, I_{thr} the minimum quantity of electricity necessary for polymerisation of the oligomer to begin under the given conditions (the intercept O–C made by the straight line in Fig. 5), which is termed a "threshold" by analogy with Lipatova and Siderko's "threshold" catalyst concentration[117], below which the anionic polymerisation of oligo(ether–acrylates) under the influence of sodium naphthalene does not take place, although the solution is

¶ Notation of oligo(ether–acrylates) taken from Ref. 118.

coloured, and K a constant representing the efficiency of the electrochemical reaction—the number of moles of the oligomer converted under the given conditions by one faraday of electricity. The value of K determined in the electrochemical initiation of the polymerisation of MGF-9 is 23.5 moles F^{-1}, indicating that the electrochemical reaction is highly efficient.

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With electrochemical initiation the electrode process is thus the source of the active centres responsible for initiating polymerisation. This allows their rate of generation to be controlled, the mechanism to be determined, and aspects of initiation to be examined in the formation of both linear and network polymers. On the other hand, the field of the electrode affects the growth of the polymer chain. The carbanion or carbonium cation carrying the chain interacts with monomer molecules already oriented in the field of the electrode. This determines the structure and the physicochemical properties of the polymers. Several publications have appeared on electrochemical initiation[122-138] while the manuscript was being prepared for the press.

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Institute of General and Inorganic Chemistry, Ukrainian SSR Academy of Sciences, Kiev

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Homolytic Substitution at the Metal Atom in Organometallic Compounds

E.B.Milovskaya

Homolytic substitution at the metal atom involves a wide range of organic derivatives of non-transition metals and takes place in reactions with free radicals where the reaction centre is located at an oxygen, nitrogen, or sulphur atom. The qualitative and quantitative aspects of these reactions have been examined. The applicability of the relations established both in the treatment of a series of reactions involving organometallic compounds and for synthetic purposes has been demonstrated. The bibliography includes 75 references.

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I. INTRODUCTION

Oxidation reactions of organic derivatives of non-transition metals have been attracting attention for a long time. These reactions are not only of theoretical but also of practical interest. In particular, the oxidation of metal alkyls leads to a convenient method of synthesising oxygen-containing compounds which are difficult to obtain otherwise; combinations of the metal alkyl-oxygen type are sometimes capable of initiating the radical polymerisation of vinyl monomers at a low temperature, etc.

The oxidation of metal alkyls takes place very rapidly, in a fraction of a minute, and since the process is heterogeneous the use of kinetic criteria to infer its mechanism proved to be difficult. Moreover, it has been established that inhibitors of free-radical reactions (hydroquinone, diphenylamine, etc.) do not affect this process. Therefore it has been suggested that the oxidation has a polar and not a homolytic mechanism. However, some authors admit the possibility of homolytic stages in the oxidation process†.

In connection with the discovery of powerful inhibitors of free-radical processes, methods for the synthesis of pure stereoisomeric forms of metal alkyls, and the application of ESR spectroscopy, in recent years it was possible to discover stages in the oxidation process which had been unknown hitherto. It was shown that the oxidation of organic derivative of boron, zinc, cadmium, aluminium, magnesium, antimony, and bismuth constitutes a bimolecular homolytic substitution at the metal atom via a mechanism of the type which obtains in S_H2 reactions‡.

In the case of polyvalent organometallic compounds, reactions of the S_H2 type proceed not only with peroxy- but also with alkoxy- and acyl radicals and with radicals in which the reaction centre is located at a nitrogen or sulphur atom.

This review deals with qualitative and quantitative aspects of the homolytic substitution reactions. Certain processes involving organometallic compounds have been analysed and it has been shown that the relations discovered may be used for preparative purposes in organic chemistry.

†The oxidation reactions and subsequent reactions of organometallic peroxides have been considered in reviews [1–3].

‡The term S_H2 reactions was introduced by Pryor [4] and was used by Davies in relation to bimolecular reactions of free radicals with the metal atom in organometallic compounds.

II. HOMOLYTIC SUBSTITUTION AT THE METAL ATOM

1. Oxidation of Organic Derivatives of the Elements

The beginning of a fundamental and systematic revision of earlier views concerning the nature of the oxidation of organic derivatives of the elements must be attributed to a study of the oxidation of 1-phenylethylboronic acid (1967), where a complete loss of stereospecificity was observed in the hydroperoxide obtained as a result of the reaction [5]. It was established that the kinetics of the oxidation of organic derivatives of boron, zinc, cadmium, aluminium, antimony, and bismuth are influenced by inhibitors of free-radical processes: galvinoxyl, nitroxide phenothiazine. An induction period, the duration of which depends on the inhibitor concentration and the nature of the metallic compound, is observed in their presence; free-radical sensitising agents (copper salts and hyponitrite) initiate the process [6–9]. The existence of a radical stage in the oxidation of organomagnesium compounds is indicated by the loss of stereospecificity and the formation of a mixture of the *exo*- and *endo*-forms of norbornylmagnesium halides having a unique composition [10].

On the basis of literature data [5,6,8–10], Davies and coworkers formulated the hypothesis that the oxidation of organometallic compounds, like the oxidation of hydrocarbons, is a radical chain process the stages of which are presented below:

$$\text{sensitisation} \xrightarrow{\text{slow}} \text{radicals}, \quad (1)$$

$$R^{\cdot} + O_2 \xrightarrow{\text{very rapid}} RO_2^{\cdot}, \quad (2)$$

$$RO_2^{\cdot} + R_nM \xrightarrow[k_p]{\text{slow}} RO_2MR_{n-1} + R^{\cdot}, \text{ chain propagation}, \quad (3)$$

$$2RO_2^{\cdot} \xrightarrow[k_{обр.}]{} \text{inactive products, chain termination}. \quad (4)$$

The mechanism shows that the stage determining the rate of propagation is the interaction between peroxy-radicals and the organometallic component [reaction (3)], alkyl radicals behaving as reaction chain transferring agents. Chain termination involves bimolecular interaction

between two peroxy-radicals leading to inactive products. The sensitisation stage will be considered below§.

Organoboron compounds are very useful for the investigation of such reactions. The bond between boron and carbon is purely covalent [14], which favours homolytic processes. In contrast to organic derivatives of aluminium or zinc, there is a wider set of stable boron alkyls available, which gives rise to a greater scope for the investigation of the oxidation reaction in this class of compounds.

A detailed kinetic study of the oxidation of a wide range of organoboron compounds yielded the quantitative characteristics of the chain propagation stage and made it possible to establish a relation between this stage and the structure of the initial boron alkyl [15,16]. It has been shown for oxydiboron derivatives, boroxins, and mono- and di-alkoxy-derivatives of boron, which are oxidised at a moderate rate, that the process is described by the relation

$$-\frac{d[O_2]}{dt} = k[BR_3]R_i^{1/2},$$

where $k = k_p/(2k_t)^{1/2}$ and R_i is the rate of sensitisation. The relation follows from Eqns. (1)–(4).

Table 1. Rate constant ratios $k_p/(2k_t)^{1/2}$ in the autoxidation of organoboron compounds [15,16] (iso-octane, 30°C).

Compound	$k_p/(2k_t)^{1/2}$, litre$^{1/2}$ mole$^{-1/2}$ s$^{-1/2}$				
	R=*n*-Bu	s-Bu	t-Bu	1-phenylethyl	benzyl
$(RBO)_3$	0.21	40	870	850	64
R_3BOR	4.4	11	—	—	—
R_3BOBR_2	43	56	—	—	—
R_3B[a]	300[b]	70[c]	—	—	300[d]

[a] In pyridine–octane mixture.
[b] $K_{eq} = 2.2 \times 10^2$ litre mole^{-1}.
[c] $K_{eq} = 0.16$ litre mole^{-1}.
[d] $K_{eq} = 8.7 \times 10^3$ litre mole^{-1}.

In a kinetic study of the oxidation of n-butyl-, s-butyl, benzyl-, and phenyl-boron derivatives, which react very rapidly, pyridine (Py), which is a powerful complex-forming agent, was introduced into the mixture. The relation established in this case is of the form

$$-\frac{d[O_2]}{dt} = k\frac{[BR_3]}{[Py]}\left(\frac{R_i}{2k_t}\right)^{1/2},$$

where $k = k_p/K_{eq}$ and reflects the following complex formation reaction:

$$BR_3 + Py \overset{K_{eq}}{\rightleftharpoons} BR_3 \cdot Py.$$

§This view has been expressed also in studies by other investigators [7,11,12]. Davies and coworkers previously held different views on the oxidation mechanism; at present this school has made the greatest experimental contribution and has obtained most of the quantitative characteristics of the mechanism described by Eqns. (1)–(4); see also Davies and Roberts [13].

This reaction results in a decrease of the initial concentration of the boron alkyl; only the non-complexed form of the alkyl is involved in the oxidation reaction. The ratios $k_p/(2k_t)^{1/2}$, i.e. the quantities corresponding to the "oxidisability" of the organoboron compounds, and the propagation rate constants are listed in Tables 1 and 2.

Table 2. Rate constants for chain propagation in the autoxidation of boron alkyls [15,16] (iso-octane), 30°C.

Compound	k_p, litre mole^{-1} s^{-1}				
	R=*n*-Bu	s-Bu	t-Bu	1-phenylethyl	benzyl
$(RBO)_3$	$1 \cdot 10^3$	$5 \cdot 10^4$	$3 \cdot 10^4$	$4 \cdot 10^6$	$1 \cdot 10^6$
R_3BOR	$3 \cdot 10^4$	$1 \cdot 10^4$	—	—	—
R_3BOBR_2	$3 \cdot 10^5$	$7 \cdot 10^4$	—	—	—
R_3B	$2 \cdot 10^6$	$8 \cdot 10^4$	—	—	$5 \cdot 10^6$
$2k_t$(ROO)	$4 \cdot 10^7$	$1.5 \cdot 10^8$	$1 \cdot 10^8$	$2.5 \cdot 10^7$	$3 \cdot 10^8$

Evidently the "oxidisability" is determined by the nature of the substituting groups; groups containing oxygen retard the oxidation, which has been attributed to an increase of electron density at boron due to oxygen: $B-OR \leftrightarrow \bar{B}=\dot{O}R$. The chain propagation rate constant does not depend quite so explicitly on the nature of the R groups.

Table 3. Rate constants for the abstraction of a hydrogen atom from organic compounds by peroxy-radicals [15].

Compound	k, litre mole^{-1} s^{-1}	°C	Compound	k, litre mole^{-1} s^{-1}	°C
Toluene	0.24	30	Phenol	$4.3 \cdot 10^3$	65
Cumene	0.18	30	2,6-di-t-butyl-4-methoxyphenol	$8 \cdot 10^4$	65
Tetralin	6.4	30	Diphenylamine	$4 \cdot 10^4$	65
Cyclohexa-1,4-diene	$1.5 \cdot 10^3$	30	*NN'*-Diphenyl-*p*-phenyldiamine	$1.9 \cdot 10^6$	65

While the ratio $k_p/(2k_t)^{1/2}$ decreases in the series n-butylboron < s-butylboron < t-butylboron, this type of relation is not observed for the chain propagation rate constant. Hence it follows that the differences between the oxidisabilities of the compounds are related mainly to changes in the chain termination rate constant¶. The relation between k_p and the nature of R is fairly complicated and reflects a number of effects which frequently act in opposition (the stability of the radical removed, the steric accessibility of the boron atom, the reactivity of the attacking radical, etc.). Table 2 shows that the rate constant for homolytic substitution at the boron atom is extremely high, particularly when compared with the abstraction of a hydrogen atom by a peroxy-radical (Table 3). Thus dealkylation of the polyvalent boron atom

¶The kinetic relations show that the chain termination is in all cases a consequence of the interaction between peroxy-radicals.

by peroxy-radicals is one of the most rapid organic reactions of the S_H2 type. The sensitisation stage is particularly complicated in self-sensitised reactions. Davies and coworkers suggest that there are three processes responsible for the formation of radicals, namely direct oxidation, which is important at the very beginning of the process, monomolecular decomposition of the peroxide formed, and finally bimolecular interaction between the oxidised and non-oxidised forms of the boron alkyl [Eqns. (5) to (7)].

$$R_3B + O_2 \xrightarrow{k_5} R_2BO_2^{\cdot} + R^{\cdot}, \quad (5)$$

$$R_3B + O_2 \rightarrow [R_2BOOR] \rightarrow [R_2BO^{\cdot} + {}^{\cdot}OR] \begin{cases} \xrightarrow[k_6]{\text{liberation from cage}} \\ \xrightarrow{\text{reaction in cage}} [R(RO)BO^{\cdot} + R^{\cdot}] \rightarrow \end{cases} \quad (6)$$

$$\xrightarrow{\text{recombination}} R(RO)_2B, \cdot$$

$$R_2BOOR \rightarrow \begin{bmatrix} R_2BO \ldots OR \\ R_3B \quad \uparrow \quad \downarrow \\ R \ldots BR_2 \end{bmatrix} \begin{cases} \xrightarrow{\text{liberation from cage}} R^{\cdot} + R_2BO^{\cdot} + R_2BOR \\ \xrightarrow{\text{recombination in cage}} 2R_2BOR. \end{cases} \quad (7)$$

The numerical values of the rate constants for the primary sensitisation steps (k_5) and for the monomolecular decomposition of certain peroxyboron compounds (k_6) are listed in Table 4.

Table 4. Rate constants for the primary sensitisation (k_5) and monomolecular decomposition of the peroxide (k_6).

Compound	10^3k_5, litre mole^{-1} s^{-1} (benzene, 25°C) (Ref.17)
R_3B	R = iso-Bu, s-Bu, cyclohexyl 0.9 1.9 21.9
R_2BOOR	10^4k_6, s^{-1} (octane, 30°C) (Ref.15)
	R = n-Bu, s-Bu 0.11 3.8

Apart from Davies, investigators who studied the polarisation of methyl methacrylate (MMA) under the influence of systems based on $BR_3 + O_2$ also pointed to reaction (7) as a source of free radicals [3,18,19]. This view is confirmed by kinetic results obtained under model conditions [11,12,15,20]. At the same time, it has been noted [15] that the experimental data at present available concerning the pathways involved in the formation of free radicals are still inadequate for final conclusions.

2. Reaction of RO· Radicals with the Metal Atom in Organometallic Compounds

The interaction of alkoxy-radicals with the central metal atom is an example of a non-chain radical substitution process. The existence of such reactions was demonstrated for the first time and then investigated by Krusic and Kochi [21] and by Davies and coworkers [22–24] using a low-temperature ESR technique (from −100°C onwards). The experiments were performed directly in the spectrometer tube containing the organometallic compound; the free alkoxy-radicals were obtained by the photolysis (P) or thermolysis (T) of t-butyl peroxide or di-t-butyl hyponitrile.

Although one might have expected under these conditions signals corresponding to the formation of products resulting from the abstraction of a hydrogen atom by RO· radicals from the solvent or from the alkyl group of the organometallic compound, analysis of the spectra showed that radicals of only one type are generated, mainly those which were incorporated previously in the metal alkyl molecule (Table 5). The results indicate the occurrence of a quite unique reaction of the RO· radical with the C–metal bond [Eqn. (8)], which had not been observed hitherto:

$$RO^{\cdot} + R_xM \rightarrow (ROMR_x)^{\cdot} \rightarrow ROMR_{x-1} + R^{\cdot}. \quad (8)$$

Table 5. The nature of the radicals formed in the interaction between RO· and MR [22,24].

MR	Method of decomposition of peroxide	Solvent	Radical detected by ESR
$ZnEt_2$	P	Tetrahydrofuran	Et
$CdMe_2$	T	Iso-octane	Me
B-n-Bu_3	P, T	"	n-Bu
B-s-Bu_3	P	t-Butyl peroxide	s-Bu
$AlMe_3$	P	Iso-octane	Me
$AlEt_3$	P	"	Et
Et_2AlOBu	P	"	Et
$SbEt_3$	P	"	Et
$BiEt_3$	T	t-Butyl peroxide	Et

It is not clear whether reaction (8) is a stepwise or synchronous S_H2 process, i.e. whether $(ROMR_X)^{\cdot}$ is a true intermediate complex or a transition stage [24]. The postulate that the reaction pathway (8) is preferable to the abstraction of hydrogen atoms is based on the greater energy gain. This follows from a comparison of the stabilities of the corresponding dissociated and formed bonds; some of the available literature data are presented in Table 6.

Table 6. Comparison of the heats of reaction ΔH between RO· and MR and between RO· and $-\overset{|}{\underset{|}{C}}-H$.

Type of bond in M–R	Bond strength, kcal mole^{-1}		ΔH	References
	M–C	M–O		
B–C	85	125	20	25,24
	70	110	40	26
Al–C	65	138	70	25,27
H–C	99	H–O 111	12	28

The energy gain in this pathway for aluminium alkyls is so great that there is actually no need for an initial decomposition of the peroxide into free radicals [22]†; we shall consider later the mechanism of this interaction.

†After this fact had been established, Davies employed in a later study a monoalkoxyaluminium derivative.

The importance of the energy parameter has been demonstrated for trialkoxyboron; in this case, the only pathway is one involving the abstraction of a hydrogen atom from the alkoxy-group with formation of the $(RO)_2BO\dot{C}HCH_3$ radical[21]. The absolute values of the homolytic substitution rate constants and the activation energies for this process have been established for a series of boron alkyls[24]. The required parameters were obtained by the method of competitive reactions in which t-BuO· radicals were able to react with BR_3 and with cyclopentane (C_5H_{10}):

$$(R'O)_2 \xrightarrow{P} 2R'O\cdot \begin{cases} \xrightarrow[k_9]{BR_3} R'OBR_2 + R\cdot & (9) \\ \xrightarrow[k_{10}]{C_5H_{10}} R'OH + C_5H_9\cdot . & (10) \end{cases}$$

(R'=t-Bu)

The concentrations of alkyl and cyclopentyl radicals were determined by ESR and k_9 was evaluated from the expression

$$\frac{k_9}{k_{10}} = \frac{[C_5H_{10}][R\cdot]}{[BR_3][C_5H_9\cdot]}$$

using the literature value of k_{10}. The relevant data (the rate constants k_9 and the activation energies E_9) are presented in Table 7.

The excited triplet form of a carbonyl compound frequently behaves like a free radical in the hydrogen abstraction reaction[4]. It has been shown[29,30] that the excited form of a carbonyl compound, like an alkoxy-radical, gives rise to homolytic substitution of the boron alkyl:

$$Me_2CO \xrightarrow{P} Me_2CO^*,$$
$$Me_2CO^* + BR_3 \xrightarrow{k_{11}} Me_2\dot{C}OBR_2 + R\cdot . \qquad (11)$$

Table 7. Absolute rate constants and activation energies for the S_H2 reaction between $(CH_3)_3CO\cdot$ radicals and boron alkyls[24] (iso-octane, 30°C).

Compound	k_9, litre mole^{-1} s^{-1}	E_9, kcal mole^{-1}
n-Bu_3B	$3\cdot10^7$	0
iso-Bu_3B	$1\cdot10^6$	1.1
s-Bu_3B	$3\cdot10^5$	4.5
$(n\text{-BuBO})_3$	$6\cdot10^5$	2.2
$(iso\text{-BuBO})_3$	$1\cdot10^6$	2.3
$(s\text{-BuBO})_3$	$6\cdot10^5$	—
$(t\text{-BuBO})_3$	$3\cdot10^6$	2.6
C_5H_{10}	k_{10} $2\cdot10^5$	E_{10} 5.2

In conformity with Eqn. (11), two signals were detected in the ESR spectra[30]. The data for the rate of the S_H2 reaction of acetone in the triplet state (Table 8) show that its reactivity in relation to boron alkyls is comparable to that of t-BuO· radicals and varies in the same sequence (cf. Table 7).

3. Interaction of Organometallic Compounds with Acyl Radicals

The interactions of organic derivatives of tin, lead, and mercury, with a number of acyl peroxides and perbenzoates, which have been investigated by Razuvaev and coworkers[31-34], are logically closely related to the reactions discussed in the preceding sections. It has been established that the interaction occurs only at the decomposition temperature of the peroxide; the products indicate the simultaneous occurrence of several processes. One of these is homolytic substitution at the metal atom by free acyl radicals formed as a result of the decomposition of the peroxide.

Table 8. Rate constants for the S_H2 reaction between acetone in the triplet state and boron alkyls at 20°C.[30]

Compound	k_{11}, litre mole^{-1} s^{-1}
Pr_3B	$1.4\cdot10^7$
$(C_6H_{13})_3B$	$8\cdot10^6$
n-Bu_3B	$7\cdot10^6$
iso-Bu_3B	$8\cdot10^4$
s-Bu_3B	$<10^4$

Organic derivatives of aluminium, thallium, and cadmium constitute a special group[35-41]. Their interaction with acyl peroxides is so vigorous that there is no necessity for a preliminary decomposition of the peroxide into free acyl radicals for homolytic substitution‡.

The interaction of AlR_3 (R = ethyl or isobutyl) with benzoyl peroxide (BP), which has been investigated in detail[35-37] both in the absence and presence of a free-radical acceptor, established a number of characteristic features of the process. The reaction is of the donor–acceptor type and is almost instantaneous down to −70°C; the stoichiometric ratio is Al:BP = 2:1. The final products are compounds corresponding to the reactions of free alkyl radicals and dialkylaluminium benzoate; only one Al–C is involved in the reaction and the yield of free radicals is about 10%. For the associated and non-associated forms of the aluminium alkyl, the reaction proceeds identically and is not accompanied by the formation of free benzoate radicals:

$$2AlR_3 + (PhCOO)_2 \rightarrow \left[\begin{array}{cc} R_3Al & AlR_3 \\ \vdots & \vdots \\ O & O \\ | & | \\ PhC \cdots O{-}O \cdots CPh \end{array} \right] \rightarrow \qquad (12)$$

$$\rightarrow 2R_2AlOCOPh + 2R\cdot \rightarrow RH,\ R_{-H},\ R{-}R.$$

The $AlEt_3$–BP interaction takes place virtually with zero activation energy and the rate constant k for the decomposition of the peroxide exceeds by many powers of 10 the rate constant for its thermal decomposition ($k \simeq 10^{-2}$ at 0°C)[42,43].

A kinetic study of the interaction between $AlEt_3$ and BP in the presence of an electron donor–ethyl acetate (EA)—showed that the rate of formation of free radicals follows the relation

$$V = k\frac{[Al]}{[EA]}[BP]^{0.5}, \text{ where } k = \frac{k_{in}}{K_{eq}},$$

‡Strictly speaking, these are trimolecular and not bimolecular reactions.

where $k = k_{in}/K_{eq}$, which corresponds to the reactions formulated below:

$$\begin{gathered} AlEt_3 + EA \overset{K_{eq}}{\rightleftharpoons} AlEt_3 \cdot EA, \\ 2AlEt_3 + BP \overset{k_1}{\rightleftharpoons} [(AlEt_3)_2 \cdot BP] \overset{k_2}{\rightleftharpoons} 2\,(Et_3AlOCOPh)^{\cdot} \rightarrow \\ \xrightarrow[\text{slow}]{k'_{in.}} 2Et_2AlOCOPh + 2Et; \quad k_{in} = k'_{in.}(k_1k_2)^{0.5}. \end{gathered} \tag{13}$$

Thus the results show that only the non-complexed form of the metal alkyl takes part in the reaction with benzoyl peroxide and the role of the electron donor reduces to the decrease of its initial concentration. As shown above, similar relations have been established also for the interaction of peroxy-radicals with R_3B in the presence of an electron donor [15,16]§.

The results obtained for triethylthallium [38,41] and diethylcadmium [40] suggest that mechanism (12) is general for this group of organometallic compounds. The driving force of the interaction is due to the enormous energy gain resulting from a number of causes: the formation of the complex leads to a weakening of the pre-existing bonds, which facilitates their dissociation, while, on the other hand, the final result of the reaction is related to the conversion of the covalent M–C bond into the ionic M–O–C–R linkage. Using $AlEt_3$–BP as an example, one may attempt to calculate the thermal balance for this interaction. By analogy with the heat of formation of a complex of $AlEt_3$ with an ester [42–44], in the formation of the complex via the two carbonyl groups of the peroxide approximately 20 kcal mole^{-1} is presumably evolved. The decomposition of the peroxide is known to require 30 kcal mole^{-1}, i.e. in the complex this process takes place almost without the consumption of heat. The stability of the AlOCOR linkage has been calculated from the formula $E = e^2/R$. If one assumes that the charge $e = 4.8 \times 10^{-10}$ e.s.u. and the distance between the charges $R = 2$ Å, [47,48] then $E \simeq 160$ kcal mole^{-1}¶. The dissociation energy of the Al–C bond (65 kcal mole^{-1}) [25] yields an overall energy gain of about 100 kcal mole^{-1}.

As already mentioned, when t-butyl peroxide interacts with $AlEt_3$, an extremely vigorous reaction also takes place [22]. The mechanism of this process is analogous to that discussed for benzoyl peroxide [Eqn. (12)]. In this case, the final product is an alkoxy-derivative of aluminium [39].

Thus homolytic substitution at the metal atom is determined by the energy gain in the conversion of M – C into M–O or M–OCOR bonds, the Lewis acidity of the metal alkyl, and the ease of dissociation of the peroxide bond. The first condition is to some extent correlated with the position of the metal in the electronegativity series, being reflected in the amount of ionic character of the bond formed. For example, boron alkyls, which contain the least "metallic" of the elements of the series considered, altogether fail to react with benzoyl peroxide [49].

§The conclusion that only the non-complexed form of $AlEt_3$ is involved in the reaction with benzoyl peroxide follows from the data obtained in a study of the kinetics of the polymerisation of vinyl chloride under the influence of the $AlEt_3$–BP system in the presence of electron donors: butyl ether, pyridine, and allyl acetate [44]. However, it has been suggested [45] that the interaction between triethylaluminium-ether and peroxides involves the displacement of one ligand by another.

¶Infrared spectra show that the Al–OCOR bond formed is ionic according to its vibration frequency [35].

4. Interaction of Metal Alkyls with Radicals having the Reaction Centre at the Nitrogen Atom

The reactions of free radicals with the reaction centre at the nitrogen atom have been investigated for the interaction of organic derivatives of boron and antimony with the dimethylnitrogen radical generated photolytically or thermally from tetramethyltetrazene [50]. Data indicating the occurrence of the following reactions have been obtained by ESR and ^{1}H NMR spectroscopy:

$$\begin{gathered} [(CH_3)_2N{-}N{=}]_2 \xrightarrow{P} \underset{(I)}{2\,(CH_3)_2N^{\cdot}} + N_2, \\ (I) + MR_x \rightarrow (CH_3)_2N{-}MR_{x-1} + R^{\cdot}. \end{gathered} \tag{14}$$

The rate constant for reaction (14) involving Bu_3B is 8×10^3 litre mole^{-1} s^{-1} at 35 °C. A similar reaction takes place with aluminium alkyls, giving a high yield of the final product, which is of preparative value for the synthesis of aluminium amides [51]. The ESR spectra for the reaction of aluminium alkyls with $(CH_3)_2N^{\cdot}$ are less definite than for alkoxy-radicals [50]. The reactions of succinimidyl radicals with organic derivatives of tin have been investigated; in the case of alkyl derivatives, the process proceeds via a radical mechanism [52]. It has been shown [53] that the interaction of R_3SnH with triazenes $Ar\underset{1}{-}N\underset{2}{=}N\underset{3}{-}N{-}R'{-}R''$ can proceed via different pathways depending on the nature of R′ and R″: either via an $S_H2(\alpha)$ reaction with formation of $R_3SnNR'R''$ or via an $S_H2(\gamma)$ 1–3 displacement reaction leading to $Ar{-}\underset{\displaystyle SnR_3}{\underset{|}{N}}{-}N{=}NR''$ and R′.

The reactions discussed in Section II, subsections 2, 3, and 4 are radical non-chain processes, i.e. a significant concentration of free radicals could be achieved in this way. For this reason, they may serve as a very convenient secondary source of free alkyl radicals with a wide variety of structures.

5. Reactions of Metal Alkyls with Radicals having the Reaction Centre at the Metal Atom

Reactions equivalent to those discussed for oxygen- and nitrogen-containing radicals obtain also with radicals where the reaction centre is at the sulphur atom. The interaction between thiophen and organic derivatives of antimony and bismuth has been investigated; thiyl radicals were generated with the aid of hyponitrile and the process was followed by NMR spectroscopy [54]. The possibility of sensitising this reaction with the aid of free radicals and of inhibiting it with phenothiazine or galvinoxyl suggested [54] that a free-radical chain process takes place, the stages of which are presented below:

$$R^{\cdot} + C_6H_5SH \rightarrow \underset{(II)}{RH} + C_6H_5S^{\cdot}, \tag{15}$$

$$(II) + MR_3 \rightarrow C_6H_5S{-}MR_2 + R^{\cdot}. \tag{16}$$

The formation of alkyl radicals following attack by sulphur-containing radicals has been demonstrated under the conditions of the photolysis of diaryl or dialkyl sulphides in the presence of boron alkyls in the tube of the ESR spectrometer [55]. The relative rates of the S_H2 reaction with participation of the organoboron compound and the reaction involving the addition of butane-1-thiol to an olefin [55] have been investigated by the method of competing reactions. The following reactivity series has been established for boron alkyls: n-Bu_3B > iso-Bu_3B > > s-Bu_3B. According to the authors, the rate of the

dealkylation reaction is determined by the steric characteristics of the butyl group. The rate constants have the same order of magnitude as for the reaction of alkoxy- or peroxy-radicals with BR_3 (10^5–10^7 litre mole^{-1} s^{-1}). The energy gain in this process is due to the difference between the stabilities of the B–S and B–C bonds, amounting to approximately 10 kcal mole^{-1}.

6. Homolytic Substitution at the Metal Atom in the Reaction with Alkyl Radicals

Homolytic substitution at the metal atom is not limited to reactions with radicals having the reaction centre at the heteroatom. Thus the kinetic parameters of the interaction of methyl radicals (produced by the photolysis of azomethane in the gas phase) with BEt_3 have been estimated [56]. The relations obtained for the two possible pathways of the process [Eqns. (17) and (18)] suggest that in this case the homolytic substitution reaction is slightly preferable to the abstraction of hydrogen:

$$CH_3^{\cdot} + BEt_3 \begin{cases} \xrightarrow{k_{17}} Et^{\cdot} + CH_3BEt_2; & k_{17}=10.6-\frac{5200}{4.58T}, \quad (17) \\ \xrightarrow{k_{18}} CH_4 + CH_3\dot{C}HBEt_2; & k_{18}=12.6-\frac{7780}{4.58T}. \quad (18) \end{cases}$$

Probably the reaction of $AlEt_3$ (or $AlEt_2Cl$ with azobisisobutyronitrile (under the conditions of the decomposition of the latter) can be classified as homolytic substitution at the metal atom by an alkyl radical; signals due to two radicals–the ethyl and dimethylcyanomethyl radicals—were detected in the ESR spectra [57].

The data presented show that reactions involving homolytic substitution at the metal atom are characteristic of a wide range of organometallic compounds. The energy gain in these reactions ensures the formation of significantly more stable bonds than those existing previously; the reactions take place with a low activation energy at a high rate, which is in many cases close to the rate determined by diffusion. Consequently, such reactions can successfully compete with other free-radical processes.

III. ANALYSIS OF CERTAIN REACTIONS INVOLVING ORGANOMETALLIC COMPOUNDS

1. Radical Polymerisation

We shall consider certain examples the interpretation of which has become possible (or more definite) on the basis of the relations discussed above. Mixtures of metal alkyls with oxygen are used as low-temperature sensitising systems, but the mechanism of the formation of free radicals under these conditions has hitherto remained fairly tentative. The reactions discussed in the first part of the review [Eqns. (5)–(7)], responsible for the formation of free radicals on oxidation, take place during the sensitisation of polymerisation under the influence of such systems. The relative contribution of reactions (5)–(7) to sensitisation is related to the nature of the metal alkyl, the relative concentrations of oxygen and the metal alkyl, temperature, etc. [2,3]

In a study of the polymerisation of methyl methacrylate in the presence of boron alkyl, it was noted that inhibitors do not affect the process. This suggested an unusual mechanism of chain propagation, involving a complex of the growing radical with the boron alkyl, which is not acted upon by the inhibitor [58,59]. It has been shown that this idea [60–62] is erroneous and the causes of the above effect have been discussed. Firstly, Arimoto [58] employed inhibitors which are in general ineffective in the polymerisation of methyl methacrylate (hydroquinone, *N*-phenyl-α-naphthylamine, etc.). The second reason is related to the specific features of the action of the usual inhibitors on boron alkyls. This phenomenon must be considered in detail, since it reflects features which are fundamentally different from those usually adopted in the chemistry of radical reactions. The interaction of inhibitors with free alkyl radicals generated in the sensitisation stage leads to the appearance of radicals with the reaction centre at oxygen or nitrogen atoms. As stated above (Section II, subsections 2 and 4), in model conditions, the reaction of radicals having such a structure with boron alkyls involves an extremely high energy gain. This leads to the formation of a new highly active alkyl radical and not a stable radical from the inhibitor. For polymerisation (M = monomer) using an inhibitor, for example quinone $C_6H_4O_2$, this is illustrated by the following mechanism [61,62]:

$$M_xM^{\cdot} + C_6H_4O_2 \rightarrow \underset{(III)}{M_xMOC_6H_4O^{\cdot}}, \quad (19)$$

$$(III) + BEt_3 \rightarrow M_xMOC_6H_4OBEt_2 + Et^{\cdot}, \quad (20)$$

$$Et^{\cdot} + M \rightarrow EtM^{\cdot}, \quad (21)$$

$$\text{etc}\dagger.$$

Thus, in a radical process involving boron alkyls (oxidation or sensitisation of polymerisation), the usual inhibitors behave at best as chain transfer agents.

All the data quoted demonstrate that only stable free radicals such as galvinoxyl or compounds generating such radicals as a result of the primary reaction (phenothiazine, nitroxide) can serve as effective inhibitors of processes involving organometallic compounds.

One may quote further examples concerning polymerisation and demonstrating that homolytic substitution at the metal atom alters the primary pattern of radical reactions. It has been established that aluminium alkyls are involved in the thermal polymerisation of styrene (St), behaving as highly active chain-transfer agents ($C_{transf} \simeq 20$) [64]. This process does not occur as a result of the abstraction of a hydrogen atom from the alkyl group but as a homolytic substitution of the entire group which had been previously linked to aluminium:

$$\text{poly-St}^{\cdot} + AlR_3 \rightarrow \text{poly-StAl}R_2 + R^{\cdot}. \quad (22)$$

Thus, instead of the relatively inactive benzyl radical, reaction (22) generates a highly active alkyl radical. Presumably the energy gain in such a reaction is associated with the stabilisation of the Al–benzyl bond relative to the Al–alkyl bond as a result of electron transfer from the benzene ring.

In the polymerisation of methyl methacrylate under the influence of systems of the type AlR_3–BP, the organoaluminium component is an extremely active chain-transfer agent [65]. Probably in this case the energetically favourable reaction between the oxygen form of the growing PMMA$^{\cdot}$ radical,

$$\sim CH_2-\underset{\underset{H_3C}{|}}{\overset{\overset{\cdot}{|}}{C}}-\underset{\underset{OR}{|}}{C}=O \leftrightarrow \sim CH_2-\underset{\underset{H_3C}{|}}{C}=\underset{\underset{OR}{|}}{C}-\dot{O},$$

†The possibility of employing a metal alkyl–hydroquinone (or quinone) mixture for the sensitisation of radical polymerisation, is also related to reactions of type (19)–(21). [63]

and the aluminium alkyl, leading to the termination of the material chain, is responsible for the observed effect.

It is well known that aluminium alkyls are themselves incapable of sensitising the polymerisation of vinyl monomers. However, when a very high concentration of $AlEt_3$ and illumination are employed, the radical polymerisation of methyl methacrylate proceeds very effectively[66]. The mechanism of the formation of free radicals is in this case probably very similar to that of reactions between the excited form of the carbonyl compound and the boron alkyl [Eqn. (11)].

2. The Applications of Reactions involving Homolytic Substitution of Groups Linked to the Metal in Synthetic Organic Chemistry

In this subsection we shall confine ourselves to a small number of examples in order to demonstrate the possibilities inherent in the process involving homolytic substitution of groups linked to the metal in preparative organic chemistry. Controlled oxidation of organoboron compounds has been used by Brown and coworkers to synthesise a wide variety of compounds. The process has a free-radical mechanism and includes a series of consecutive reactions at the boron atom with participation of $R_2^{\cdot}$, $RO^{\cdot}$, and $RS^{\cdot}$ radicals [67-73,75].

Conditions for the quantitative oxidation of organoboron compounds to the corresponding alcohols have been found[67]. It has been stated that the reaction is appreciably inhibited by a small amount of iodine[68]. The oxidation of Bu_3B in the presence of organic iodides R'I' (R' = benzyl, allyl, *p*-nitrobenzyl, etc.) leads to the formation of butyl iodide in an amount equivalent to that of the initial iodide and of the recombination products of the R'' radicals[69]. Reactions responsible for the observed course of the process have been suggested:

$$R_3B + O_2 \rightarrow R_2BO_2^{\cdot} + R^{\cdot}, \quad (23)$$

$$R^{\cdot} + R'I \rightarrow RI + R''^{\cdot}, \quad (24)$$

$$2R''^{\cdot} \rightarrow R'—R', \quad (25)$$

$$R''^{\cdot} + O_2 \rightarrow R'O_2^{\cdot}, \quad (26)$$

$$R'O_2^{\cdot} + R_3B \rightarrow R'O_2BR_2 + R^{\cdot}. \quad (27)$$

$\alpha\beta$-Unsaturated aldehydes or ketones with an external double bond are known to undergo a 1,4-addition reaction with boron alkyls, giving rise to saturated carbonyl derivatives[70]. The process is inhibited by galvinoxyl radicals. This led to the assertion that it has a homolytic mechanism; earlier it was believed that the reaction has a polar mechanism with a six-membered transition state[71]. In the absence of specially introduced sensitisers, unsaturated β-substituted carbonyl compounds are incapable of this type of reaction with boron alkyls. The presence of a measurable amount of oxygen (or of other free-radical sensitisers) ensures the development of the process in the required direction and the yield of the desired product is close to theoretical. The intermediate stages of this reaction (for methyl propenyl ketone) are quoted below[72]:

$$BR_3 + O_2 \rightarrow R^{\cdot}, \quad (28)$$

$$R^{\cdot} + CH_3CH{=}CH{-}CO{-}CH_3 \rightarrow \underset{\displaystyle CH_3CH{-}CH{=}CO{-}CH_3}{\overset{\displaystyle R}{\overset{|}{CH_3CH{-}\dot{C}H{-}CO{-}CH_3}}}, \quad (29)$$

(IV)

$$(IV) + BR_3 \rightarrow \overset{\displaystyle R}{\overset{|}{CH_3CH}}{-}\overset{\displaystyle CH_3}{\overset{|}{CH}}{=}CO{-}BR_2 + R^{\cdot}, \quad (30)$$

$$\xrightarrow{\text{hydrolysis}} CH_3\overset{\displaystyle R}{\overset{|}{C}}H{-}CH_2{-}\overset{\displaystyle CH_3}{\overset{|}{C}}{=}O. \quad (31)$$

The synthesis of homologues of the tetra-atomic carbon chain, achieved by the interaction of the monoepoxy-derivative of buta-1,3-diene with the boron alkyl, is closely related to these reactions [reactions (28)–(31)].[73]

It has been established that the reaction of organic derivatives of boron with mercaptans hardly occurs in the absence of oxygen or peroxy-compounds. In the presence of free-radical sensitising agents, the process proceeds at a high rate and leads to the formation of dialkylthioboronic acids and saturated hydrocarbons[74]. A convenient synthesis of organic sulphides from disulphides and boron alkyls has been proposed by Brown and Midland[75].

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The review can be aptly concluded by Davies' words[13]: "Reactions of the bimolecular homolytic substitution type take place readily at a metallic centre, particularly where the displaced group is an alkyl radical. This provides a new context for investigating the behaviour of free radicals, and is the key to the understanding of many organometallic reactions".

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Institute of Macromolecular Compounds,
USSR Academy of Sciences, Leningrad

U.D.C. 547.303/.306

The Properties of Orthoesters and Their Applications in Organic Synthesis

V.V.Mezheritskii, E.P.Olekhnovich, and G.N.Dorofeenko

A systematic and general account is given of data on the properties of orthoesters and their applications in organic synthesis. The mechanisms of certain reactions involving orthoesters have been considered or revised.
The bibliography includes 278 references.

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I. INTRODUCTION

Despite the fact that the esters of orthocarboxylic acids cannot always be compared as regards the number of known examples with certain widely familiar classes of organic compounds, their importance in many synthetic methods is very great. It is sufficient to say that the application of orthoesters made it possible to develop extremely simple methods for the introduction of the formyl or acyl residue into an aromatic ring, at a double bond, and in the α-methyl and methylene groups of carbonyl and heterocyclic compounds. Acylation and also alkylation of oxygen, sulphur, nitrogen, phosphorus, and silicon atoms of a wide variety of organic and inorganic substances has been achieved with the aid of orthoesters.

It is noteworthy that hitherto orthoformates (in particular ethyl orthoformate) have found the greatest number of applications, which is due to their high reactivity in many reactions and greater availability compared with other orthoesters.

The advances achieved in the chemistry of aliphatic orthoesters were described in Post's review[1] published in 1943. In 1953, the properties of ethyl orthoformate were briefly reviewed[2]. Certain examples of the applications of orthoesters have been compared in familiar monographs on organic chemistry[3-5]. However, there are no reviews in the Soviet literature dealing with this problem.

The vigorous development of the chemistry of orthoesters in recent years led to the accumulation of extensive factual data, a systematic and general account of which is required. Moreover, the mechanisms of certain reactions have been re-examined and revised in the light of recent studies.

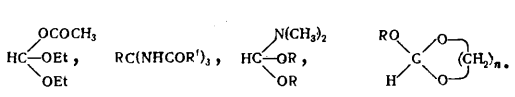
In the present review, we attempted to cover the known types of reactions of orthoesters without endeavouring to give an exhaustive description of data for individual reactions.

II. THE STRUCTURE AND REACTIVITY OF ORTHOESTERS

Organic orthoesters have the general formula (I) and are the esters of orthoacids which do not exist in a free state:

$$RC(XR')_3.$$
(I)

Oxygen or sulphur function as the heteroatom X. The group R can be an alkyl, aryl, or aralkyl residue or a functional group (COOR, OR, etc.). The group R′ is as a rule aliphatic, although aryl orthoformates are known[6]. There exist mixed orthoesters containing groups R′ of different types. These include, for example, diethoxymethyl acetate (II)[7]. Certain amino-derivatives of orthoacids [orthoamides(III)][8], acetals of dimethylformamide (IV)[9], cyclic orthoesters (V)[10], etc. resemble orthoesters as regards the nature of the reactions in which they are involved.

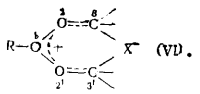


(II) (III) (IV) (V)

Orthoesters are highly reactive owing to the electron deficient central carbon atom caused by the $-I$ effect of the electronegative groups XR. The presence of a positive charge on the central atom results in their affinity for nucleophilic agents and the transition state is stabilised fairly readily by the elimination of HXR (an alcohol or mercaptan).

Orthoesters can be activated by protic and aprotic acids. The catalytic effect of acids is due to their interaction with orthoesters, which gives rise to the formation

under the reaction conditions of an extremely reactive carboxonium ion (VI), which has been isolated as a salt [10]:



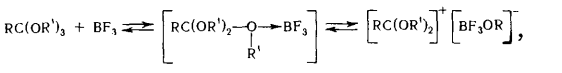
(VI).

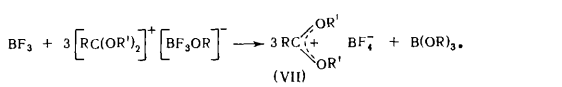
As a result of [electron] delocalisation, the dialkoxycarboxonium cation carries a partial positive charge both on the oxygen atoms and on the carbon atoms linked to them (1,3,3′). As a result of such charge distribution, the carboxonium ion exhibits a dual reactivity. In those cases where the nucleophilic centre of the reacting species is attacked by the central carbon atom of the carboxonium ion, insertion into the molecule of the acetal fragment $RC(OR')_2$, i.e. acylation, takes place. On the other hand, when the attack is by the 3- or 3′-carbon atom of the alkyl group, alkylation takes place. Acylation can occur both at a carbon atom in organic compounds (the formation of a C–C bond) and at a heteroatom (O, S, N, P, etc.). Alkylation is as a rule directed only to a heteroatom which is involved in a multiple bond (=O, ≡N, =S, etc.). However, cases of alkylation at S–H or O–H bonds are known [11,12], as well as cases where an alkyl group combines with a halide ion [13,14]. Under certain conditions acylation and alkylation reactions can occur simultaneously and behave therefore as competing or parallel processes [15]. Under conditions of acid catalysis, the orthoesters of alkanecarboxylic acids give a lower yield of condensation products with amines [16] and ketones [7] than orthoformates. This can be accounted for by the compensation of the positive charge of the carboxonium ion produced by the $+I$ effect of the alkyl group.

The specific effect of the structure of the orthoester on its reactivity is discussed in the individual sections of the review.

III. REACTIONS OF ORTHOESTERS WITH INORGANIC ACIDS

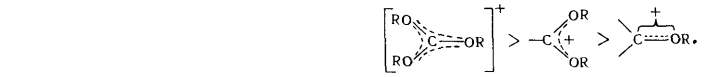
Orthoesters react with protic and aprotic acids, metal halides, and certain oxides. Acids and metal halides (calcium, magnesium, platinum, antimony, etc. halides) tend to form complexes which are sometimes fairly stable and can be isolated. Meerwein [10] showed that orthoesters form complexes with BF_3 and $SbCl_5$, which in certain cases can ionise at the C–O bond with formation of a carbonium ion and the complex anions $(ROBF_3)^-$ or $(ROSbCl_5)^-$, disproportionating to the stable anions BF_4^- and $SbCl_6^-$:



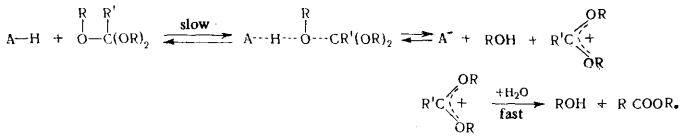


(VII)

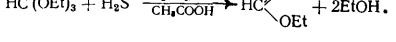
The anion disproportionation stage is rate-limiting. The capacity of the complexes for ionisation increases with electron density at the central atom and with increase of the stability of the carboxonium ion (VII) formed. In the general case, the stability of carboxonium ions decreases with the number of oxygen atoms bound to the charged carbon atom, owing to the decrease of the contribution of the oxonium forms to the corresponding carboxonium structure:



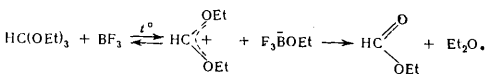
The hydrolysis of orthoesters is one of the most thoroughly investigated reactions. Many studies have been made on the elucidation of its mechanism. In the light of recent data [18–20], the hydrolysis of orthoesters is an example of general acid catalysis reaction and may be regarded as an example of bimolecular electrophilic S_E2 substitution at the oxygen atom:



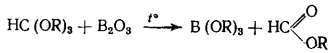
The reaction of ethyl orthoformate with hydrogen sulphide takes place similarly to hydrolysis [21]:



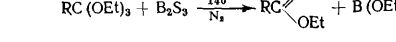
When ethyl orthoformate is heated in the presence of very small amounts of BF_3, it undergoes catalytic decomposition into ethyl formate and ethyl ether [22]:



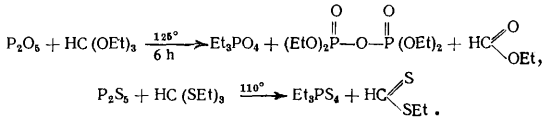
Acidic oxides are alkylated by orthoesters at the oxygen atom. Evidently this process also involves the formation of a carboxonium ion, since the reaction products include ethers and esters. When a 1 : 3 mixture of boron trioxide and an alkyl orthoformate is heated, trialkyl borates are formed [23] in yields of about 50%:

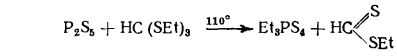


Under more severe conditions, boron trisulphide also reacts with orthoesters:



Reactions of ethyl orthoformate and ethyl thio-orthoformate with phosphorus pentoxide and pentasulphide have been described [25]:





The reactions of orthoesters with metal and non-metal halides have been investigated. These reactions usually result in the substitution of halogen atoms by alkoxy-groups. The reaction products may include alkyl halides, ethers, and carboxylic acid esters. Thus Arbuzov and Bogonostseva [26], who investigated the reaction of phosphorus trichloride with ethyl orthopropionate, observed that, by altering the proportions of the reactants, it is possible to replace in succession all three halogen atoms in the PCl_3 molecule by ethoxy-groups.

In the presence of $AlCl_3$, germanium tetrachloride reacts with orthoformates [27] to form substances having the general formula $Cl_nGe(OR)_{4-n}$, where $n = 0-3$.

The capacity of orthoesters to give rise to alkyl halides in the presence of halide ions has been used in the synthesis of ethyl fluoride [14], which is formed in 90% yield.

A novel method of synthesising alkyl iodides, proposed by Dangiyan [13], is based on the interaction of alkyl orthoformates with elemental iodine in the presence of various metals (Mn, Zn, Mg, Fe, Al).

The reactions of orthoesters with halogen-containing organic derivatives of the elements have been investigated. A method of preparing alkoxysilanes by the reaction of halogenosilanes with alkyl orthoformates in the presence of $AlCl_3$ has been described [28]:

$$R_mH_nSiX_{4-(m+n)} + HC(OR')_3 \xrightarrow{AlCl_3} R_mH_nSi(OR')_{4-(m+n)}$$

($m = 0, 1, 2, 3$; $n = 0, 1, 2, 3$; $m + n \leqslant 3$, X = halogen). Chlorocyanoalkylsilanes [29], boron-containing chloroalkylsilanes [30], and 1,1,1-trihalogenophospholens [31] are alkoxylated similarly.

A convenient method for the alkylation of phosphorodithioic acid ester consists in heating in with the orthoesters of alkanecarboxylic acids:

$$(EtO)_2P(S)SH + RC(OR')_3 \rightarrow (EtO)_2P(S)SR' + R'OH + RC(O)OR'.$$

The alkylation reaction also constitutes the basis of the synthesis of alkyl hypophosphites from hypophosphoric acid [12]:

$$H_2P(O)OH + RC(OR')_3 \xrightarrow{N_2} H_2P(O)OR' + R'OH + RC(O)OR'.$$

An interesting method of formylation at a phosphorus atom consists in heating a mixture of orthoformate and dialkyl metaphosphate [32]:

$$(RO)_2P(O)H + HC(OR')_3 \rightarrow (RO)_2P(O)CH(OR')_2 + R'OH.$$

IV. EXCHANGE OF ALKOXY-GROUPS AND ALKYLATION REACTIONS

1. Exchange of Alkoxy-groups of Orthoesters

Transesterification reactions leading to partial or complete replacement of alkoxy- or alkylthio-groups of the orthoesters by new RO or RS groups may be regarded as the simplest reactions of orthoesters. These reactions take place when orthoesters are treated with alcohols, phenols, carboxylic acids, carboxylic acid anhydrides, and mercaptans and are typical examples of nucleophilic substitution at a saturated carbon atom.

Transesterifications with alcohols, phenols, and mercaptans as a rule requires an active catalyst, while in the case of carboxylic acids the latter probably are sufficiently acidic to catalyse the reaction. The reactions involve a carboxonium ion:

$$RC(XR')_3 + H^+ \rightleftharpoons RC^+(XR')_2 + R'XH,$$

$$RC^+(XR')_2 + R''YH \rightleftharpoons R''\overset{+}{Y}(H)-C(XR')_2R \rightleftharpoons RC(XR')(YR''),$$

$$RC(XR')_2(YR'') \overset{+R''YH}{\rightleftharpoons} RC(XR')(YR'')_2 \overset{+R''YH}{\rightleftharpoons} RC(YR'')_3.$$

The exchange of alkoxy-groups constitutes the basis of the synthesis of higher alkyl orthoformates, which are obtained in yields of 75–95%. [33,34]

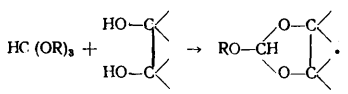
The corresponding orthoformates are also produced when a mixture of ethyl orthoformate is refluxed with ethyl or butyl alcohol in the presence of $ZnCl_2$. [35] If zinc chloride is replaced by sulphuric acid, another reaction takes place:

$$HC(SEt)_3 + 3BuOH \xrightarrow{H_2SO_4} 3EtSH + HC(O)OBu + (Bu)_2O.$$

β-Chloroalkanols react with orthoformates, giving rise to a 54–88% yield of β-chloroalkyl orthoesters [36]. Aryl orthoformates have been obtained similarly [6,37].

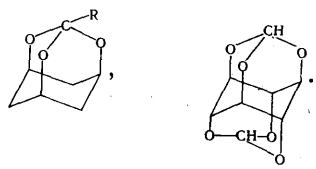
Mercaptans can react with orthoesters even at room temperature. The products are thio-orthoesters produced in nearly quantitative yields [38].

Compounds containing two or three hydroxy-groups also react with orthoesters, giving rise to the corresponding cyclic derivatives. Ethylene glycol and its derivatives [methylethylene glycol, glycerol α-chlorohydrin, pinacol, cyclohexane-1,2-diol, (+)-tartaric and mesotartaric acids, etc.] give rise to 2-alkoxy-1,3-dioxolanes on heating with methyl or ethyl orthoformates [39,40]:

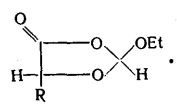


Glycerol and polyhydric alcohols behave similarly.

In the presence of BF_3, *cis*-phloroglucitol reacts with ethyl orthoformate and ethoxycarbonyltriethoxymethane [41,42], the oxa-analogues of adamantane being formed in yields in excess of 70%:



The syntheses of cyclic orthoesters of sugars [43], steroids [44], and other complex compounds have been described. On heating in benzene in the absence of a catalyst, ethyl orthoformate reacts with hydroxyacids [45]. 2-Ethoxy-1,3-dioxolan-4-ones (VIII) were obtained in high yields by this procedure:



(VIII)

In the presence of BF_3, oxiran or methyloxiran adds to methyl or ethyl orthoformate with formation of adducts differing in the proportion of alkoxy-groups [46]:

$$HC(OR)_3 + CH_2(O)CH_2 \xrightarrow{BF_3} HC(OR)_n[(OCH_2CH_2)_mOR]_{3-n}.$$

(n=0, 1, 2; m=1, 2, 3)

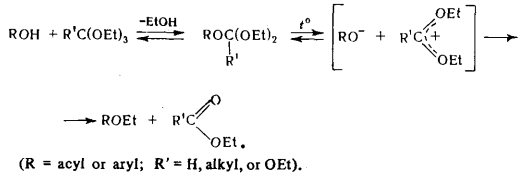
Post and Erickson [47] observed that, when carboxylic acid anhydrides are allowed to react with orthoesters, an alkoxy-group is replaced by an acyloxy-group:

$$RC(OEt)_3 + (R'CO)_2O \rightarrow RC(OEt)_2OCOR' + R'C(O)OEt.$$

This reaction takes place only at elevated temperatures and is irreversible.

2. Alkylation Reactions

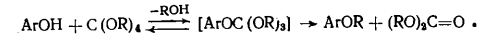
Orthoesters are used to alkylate carboxylic acids, phenols, and certain amines. When acids and phenols are alkylated, the usual transesterification of the orthoesters probably takes place initially. This is followed by the thermal dissociation of the newly formed RO–C linkage and alkylation of the RO^- anion by a carboxonium ion (see Section II):



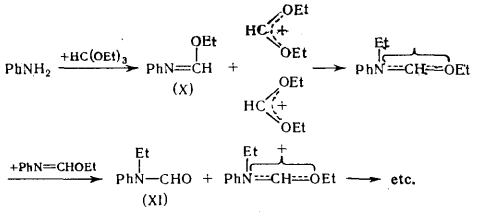
(R = acyl or aryl; R' = H, alkyl, or OEt).

The esterification of carboxylic acids by orthoesters is very promising for preparative purposes [49]. The method is applicable to the esterification of aliphatic, aromatic, and sterically hindered acids as well as certain acids which are difficult to esterify.

Smith [37] obtained alkyl ethers of phenols by refluxing mixtures of the corresponding phenol with a small excess of orthocarbonate:



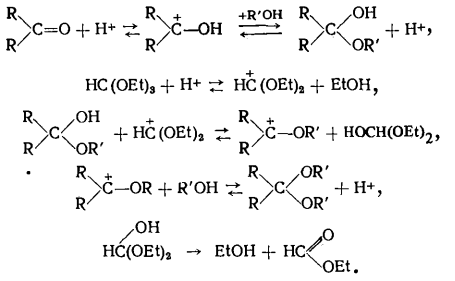
An interesting reaction was discovered by Roberts and Vogt [50], who showed that, when aniline is heated with ethyl orthoformate in the presence of sulphuric acid above 140°C, the aniline is *N*-alkylated. The ethyl ether of *N*-phenylformamide (X) is formed initially and then *N*-ethylformanilide (XI):



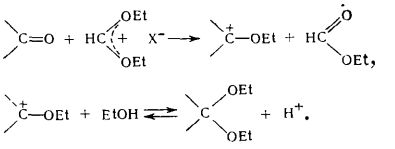
Compound (X) can be converted into (XI) also in the absence of orthoesters but the presence of the latter increases the yield of (XI). When compound (X) is treated with sulphuric acid and isopentyl orthoformate, a mixture of *N*-ethyl- and *N*-isopentyl-formanilides is formed. Toluene-*p*-sulphonic acid also catalyses this reaction but the yield of compound (XI) is low, while the reaction with HCl does not occur at all. These findings are consistent with the sequence of reactions expressed by the above mechanism, which takes into account the intermolecular nature of the conversion of compound (X) into (XI). The method of Roberts and Vogt can be recommended for the synthesis of *N*-monoalkylanilines via the corresponding formanilides in high yields [51,52].

V. SYNTHESIS OF ACETALS AND ENOL ETHERS

The method of synthesising acetals and ketals from the corresponding carbonyl compounds, orthoformates, and alcohols was developed by Claisen [53] and was subsequently widely adopted. The formation of acetals and ketals is an acid-catalysed reaction; it is assumed that the alcohol and not the orthoester behaves as a donor of alkoxy-groups [54]:



Kabuss [55] and Dimroth and Heinrich [56] observed that diethoxycarbonium salts obtained by Meerwein's method [10] from ethyl orthoformate are highly active alkylating agents. In particular, when these salts are mixed with aldehydes or ketones, the latter are *O*-ethylated with formation of ethoxycarbonium salts in nearly quantitative yields. This means that direct interaction between dialkoxycarbonium ions and the carbonyl compound is possible:



Naturally it is probable that the reaction proceeds simultaneously via the two mechanisms indicated with formation of the same final products.

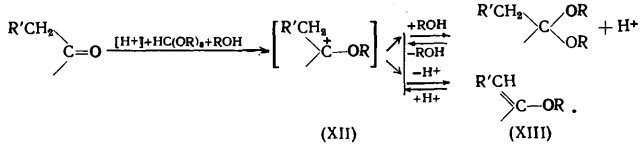
Hydrochloric, sulphuric, phosphoric, and toluene-*p*-sulphonic acids, ammonium chloride, sulphate, or nitrate, iron chloride, and other reagents are used as catalysts for the synthesis of acetals and ketals. Catalysts such as ammonium sulphate and nitrate and the hydrochlorides of mono-, di-, and tri-ethylamines are more effective than ammonium chloride. Magnesium and zinc chlorides give satisfactory results. Alkali metal chlorides are ineffective. Organic acids also exhibit catalytic activities but much weaker than inorganic acids. Their catalytic activity decreases in the sequence oxalic acid > formic acid > > acetic acid.

Ethyl orthoformate is usually employed to synthesise acetals. Other alkyl orthoformates give lower yields and ethyl orthoacetate does not react at all [57]. Benzaldehyde and its substituted derivatives form acetals in nearly quantitative yields regardless of the nature of the substituent [53,58]. Ketals of aliphatic-aromatic ketones such as acetophenone are obtained in yields up to 90% [54,59]. Acetals of aliphatic [58] and $\alpha\beta$-unsaturated aldehydes and ketones are formed in lower yields (which do, however, reach 80%) [60,61].

The rate of formation of ketals decreases with increase of the molecular weight of the ketone. Ketones with a branched hydrocarbon chain react more slowly than those with straight-chain alkyl groups and t-butyl methyl ketone does not react at all with orthoformate ester [3,62].

The questions concerning the synthesis of acetals and ketals have been described in detail in monographs by Post [1] and Houben [3] and partly in other publications [2,4,5].

The formation of enol ethers via an elimination reaction probably competes with the formation of acetals:

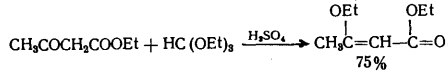


(XII) (XIII)

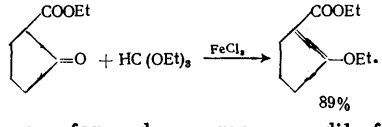
The mechanism shows that the synthesis of acetals and enol ethers invariably involves the intermediate formation of a carboxonium ion (XII). Since acetals and vinyl ethers are products of competing reactions, they are as a rule present together, their relative amounts depending on the process conditions and the structure of the carbonyl component.

The presence of an electronegative group at the α-carbon atom of the carbonyl compound increases the mobility of the α-methylene hydrogen atoms and thereby facilitates the conversion of the carbonium ion (XII) into the vinyl ether (XIII). The ease of formation of enol ethers is satisfactorily correlated with the tendency of the carbonyl compound to enolise. Favourable conditions for the formation of vinyl ethers are created when a mixture of orthoester and the carbonyl compound is heated for a long time in the presence of acids. In this instance, the action of toluene-*p*-sulphonic acid is most specific.

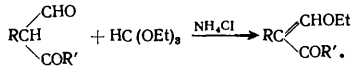
Enol ethers are formed extremely readily from β-dicarbonyl compounds, which is caused not only by the greater acidity of the α-methylene hydrogen atoms but also by the appearance of the group $O{=}C{-}C{=}C{-}OR$, which contains conjugated double bonds. Thus β-ethoxycrotonate is obtained from acetoacetic ester in the presence of several drops of sulphuric acid [63]:



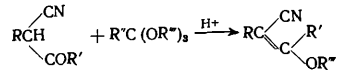
Esters of cyclic β-ketoacids react similarly [64]:



Enol ethers are formed even more readily from β-ketoaldehydes [65,66]:

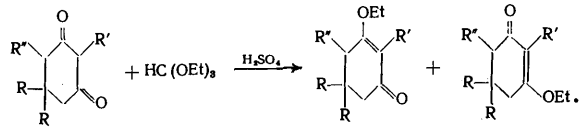


The highly electronegative cyano-group can activate the methylene group [67]:

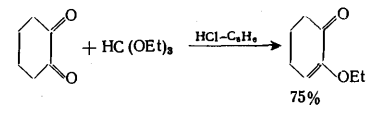


(R and R′ = H, alkyl, or aryl; R″ = H or alkyl; R‴ = alkyl).

Cyclic ketones show a greater tendency towards the formation of enol ethers than open-chain compounds. A general method for synthesising monoenol ethers of substituted cyclohexane-1,3-diones has been described [68]:

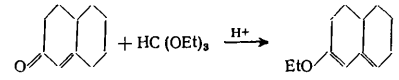


The monoenol ether of cyclohexane-1,2-dione can be obtained in solution in benzene saturated with hydrogen chloride [69]:



The conjugation of the keto-group with a benzene ring facilitates the formation of cyclic enol ethers. Thus an enol ether is formed from α-tetralone even at room temperature [70].

When enol ethers are produced from non-aromatic polycyclic compounds, the new double bond is formed in such a way that a conjugation chain is created (or preserved). This usually involves the migration of the existing double bond. As an example, one may quote the reaction of ethyl orthoformate with $\Delta^{1,9}$-2-octalone [71]:

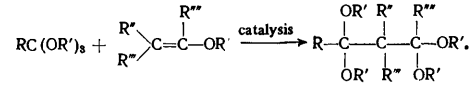


The formation of enol ethers with simultaneous migration of the double bond is very typical of steroids [72,73].

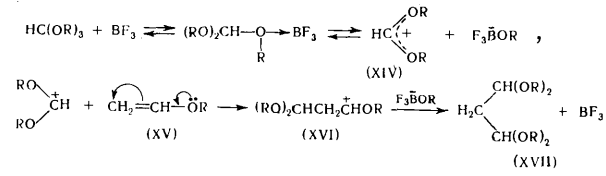
VI. REACTIONS WITH VINYL ETHERS AND THEIR ANALOGUES

The reaction of orthoesters with vinyl ethers has been described in detail in a highly informative review by Povarov [74]. This section gives a brief description of the general properties of this reaction, attention being concentrated on the reaction of orthoesters with analogues of vinyl ethers involving a similar mechanism.

The overall reaction of orthoesters with vinyl ethers can be represented schematically as follows:



This process, which takes place in the presence of acid catalysts (BF_3, $ZnCl_2$, $FeCl_3$, etc.), can have an ionic mechanism similar to that proposed for the analogous reaction of acetals [75]:



In the course of this reaction, as in many of the cases discussed above, a reactive dialkoxycarbonium ion (XIV) is formed and attacks the β-carbon atom of the vinyl ether (XV), the double bond of which is activated owing to the $+M$ effect of the alkoxy-group. As a result, the acetal fragment ($-HC(OR)_2$) is inserted into the molecule of the vinyl ether with subsequent addition of the alkoxy-group to the carbonium ion (XVI). The final products (XVII) are tetra-acetals of β-dicarbonyl compounds.

The cationic polymerisation of vinyl ethers is an undesirable competing process. Moreover, the carbonium

ion (XVI) can react further with the vinyl ether, which results in the formation of high-molecular-weight adducts. However, since the reactivity of the cation (XIV) is usually higher than that of the cation (XVI), the reaction proceeds preferentially with formation of the tetra-acetal (XVII) even when the molar ratio of the components is 1 : 1 and does not depend very markedly on the amount of the orthoester [76]. Nevertheless, in order to ensure higher yields of the monoadducts (XVII), it is better to employ an excess of the orthoester. In the presence of an excess of the vinyl ether, adducts with higher molecular weights can also be isolated, for example 1,1,3,5,5-pentaethoxypentane [76]:

$$HC(OEt)_3 + 2CH_2{=}CHOEt \xrightarrow{BF_3} EtOCH[CH_2CH(OEt)_2]_2.$$

Povarov [74] showed on the basis of the literature data that orthoesters are intermediate between saturated and $\alpha\beta$-unsaturated acetals as regards reactivity in the above reactions and resemble aromatic acetals. Therefore orthoesters form readily and in high yields monoadducts with unsubstituted and β-substituted vinyl ethers. In the reaction with the more reactive α-alkyl-substituted vinyl ethers, the yield of monoadducts falls approximately by a factor of two and the yield of polymeric products increases. Finally, in the reaction with the highly reactive alkoxydienes, cationic polymerisation predominates and adducts of orthoesters are not formed at all. As was to be expected, in the reactions with vinyl ethers (see Section II) orthoformates are more reactive than orthoacetates [77].

Among the wide variety of tetra-acetals obtained by the reaction of orthoesters with vinyl ethers, one should distinguish the tetra-acetals of malonic dialdehyde, which are difficult to obtain by other methods and which are important intermediates in many syntheses of heterocyclic systems. A simple method of preparation of the tetra-acetals of malonic dialdehyde from readily available compounds consists in the condensation of vinyl acetate with ethyl orthoformate, which involves the exchange of the acetoxy-group for an ethoxy-group [78]:

$$HC(OEt)_3 + CH_2{=}CHOCOCH_3 \xrightarrow{FeCl_3} H_2C\begin{matrix}CH(OEt)_2\\CH(OEt)_2\end{matrix}\ (60\%).$$

Thio-orthoesters react similarly with vinyl ethers [79] and vinyl sulphides [80]:

$$HC(SEt)_3 \xrightarrow{CH_2{=}CHOR} (EtS)_2CHCH_2CH\begin{matrix}OR\\SEt\end{matrix}$$

$$HC(SEt)_3 \xrightarrow{CH_2{=}CHSR} (EtS)_2CHCH_2CH\begin{matrix}SR\\SEt\end{matrix}.$$

Nitrogen analogues of orthoesters and enamides undergo a similar reaction [81]:

$$HC(NHCOOEt)_3 + R'CH{=}CHNHCOOEt \rightarrow R'CH[CH(NHCOOEt)_2]_2.$$

The reaction of orthoesters with ketones in the presence of Friedel–Krafts catalysts leads to the formation of dialkylacetals of β-keto-aldehydes [15, 82]. The enolic form of the ketone (XVIII) plays the role of the vinyl ether in this reaction. The essential features of the reactions can be traced using as an example the interaction between ethyl orthoformate and acetophenone, which gives rise to the diethylacetal of benzoylacetaldehyde (XX):

$$HC(OEt)_3 + HClO_4 \rightleftarrows \overset{+}{H}C(OEt)_2ClO_4^- + EtOH,$$

$$PhC(OH){=}CH_2\ (XVIII) + \overset{+}{H}C(OEt)_2 \rightleftarrows Ph{-}\overset{+}{C}H{-}CH_2CH(OEt)_2\ (XIX) \xrightleftharpoons{-H^+} PhCOCH_2CH(OEt)_2\ (XX,\ 30\%).$$

A characteristic feature of this reaction is that the intermediate cation (XIX) is not stabilised by the addition of an RO radical, as for vinyl ethers, but by the dissociation of a proton. This gives rise to a dimethylacetal of the β-dicarbonyl compound instead of the tetra-acetal. The formation of ketals is a competing reaction.

All the above reactions of orthoesters with ketones in an acidic medium can be described by an overall general mechanism. For simplicity, the reversibility of the reaction is not indicated:

$$-H_2C{-}C(=O){-}H \xrightarrow[+H^+\downarrow\uparrow -H^+]{+\overset{+}{C}H(OR)_3} \left[-H_2C{-}\overset{+}{C}(OR){-}\right] \begin{matrix}\xrightarrow{+ROH} -H_2C{-}C(OR)_2{-}\\ \xrightarrow{-H^+} -HC{=}C(OR){-}\end{matrix}\ \text{pathway } A.$$

$$\left[-H_2C{-}\overset{+}{C}(OH){-}\right] \xrightarrow{+ROH} \left[-H_2C{-}C(OR)_2{-}OH\right], \quad (+\overset{+}{C}H(OR)_3)$$

$$-CH{=}C(OH){-} \xrightarrow[-H^+\downarrow\uparrow +H^+]{+\overset{+}{C}H(OR)_3} \left[(RO)_2CH{-}CH(OR){-}\overset{+}{C}(OH){-}\right] \xrightarrow{-H^+} -HC(CH(OR)_2){-}C(=O){-}\ \text{pathway } B.$$

Thus the dual reactivity of dialkoxycarbonium ions is revealed by the fact that they are capable of *O*-alkylation (pathway *A*) with formation of ketals (or enol ethers) and of *C*-formylation, or more precisely of inserting the fragment $HC(OR)_2$ with formation of β-ketoacetals (pathway *B*).

The nature and relative amounts of the final products are greatly influenced by the amount of the acidic reagent. In the presence of catalytic amounts of acids, the reaction could be carried out with a limited number of ketones [17]. Apart from the diethylacetal of benzoylacetaldehyde (XX), low yields are obtained also of the diethylacetals of *p*-methoxy- and *p*-ethoxy-benzoylacetaldehydes.

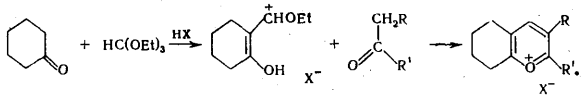
The reaction with aliphatic and alicyclic ketones usually cannot be arrested at the stage of a monoadduct of type (XX), more far-reaching transformations taking place. Thus the condensation of two molecules of a ketone with an orthoester in the presence of molar amounts of acid results in the formation of a 1,5-diketone, which cyclises under the reaction conditions to a pyrylium cation:

$$RCOCH_3 + HC(OR')_3 \xrightarrow{H^+} RCOCH_2CH(OR')_2 \xrightarrow{+RCOCH_3} \rightarrow \begin{matrix}OR'\\CH\\CH_2\ (RCO)\end{matrix}\ \begin{matrix}CH_2\ (OCR)\\\xrightarrow[-R'OH;\ -H_2O]{+HX}\end{matrix}\ \left[R{-}\overset{+}{O}{=}C(R){-}R\right]\ X^-.$$

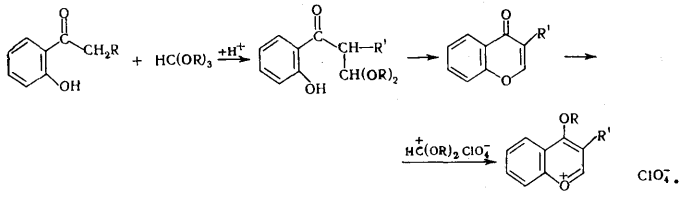
This reaction has served as a basis for a method of synthesising pyrylium salts, which is of general validity. The acid reagents employed are 70% perchloric and 98% sulphuric acids, boron trifluoride-ether, dry hydrogen chloride, aluminium chloride, iron(III) chloride, and others [83].

It has been shown [17] that orthoformates are the most reactive in this process. The yields of pyrylium salts decrease with increase in the chain length of the alkyl substituents in the orthoformate molecule. Orthoesters of alkanecarboxylic acids form [pyrylium] salts in low

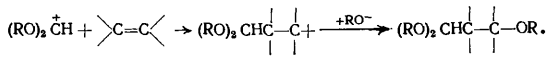
yields. Aliphatic-aromatic, alicyclic, and certain aliphatic ketones enter into the reaction. The yields of pyrylium salts are as a rule high. Cross-condensation was achieved with alicyclic ketones [84]:



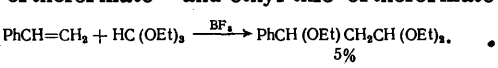
When alkyl *o*-hydroxyaryl ketones are employed, the intermediate acetals of β-ketoaldehydes are probably initially cyclised to chromones, which are alkylated and converted into 4-alkoxychromylium salts. The latter are hydrolysed to give high yields of chromones and isoflavones (including natural products of this structure [17,85,86]:



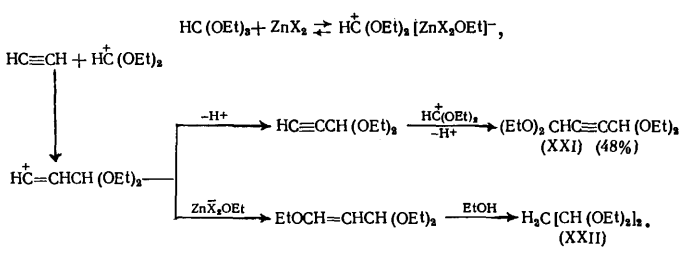
The mechanism of the reaction of vinyl ethers with orthoesters can be quite legitimately applied to the reaction of orthoesters with olefins. The only difference is that the addition to one of the carbon atoms at the double bond is not due to the activating and directing influence of the alkoxy-group, as in vinyl ethers, but is due to the polarisation of the double bond induced by the carbonium cation:



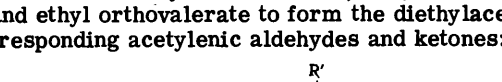
Orthoesters are known [87] to add to isobutene and cyclopentadiene. In the presence of BF_3, styrene condenses with ethyl orthoformate [77] and ethyl thio-orthoformate [87]:



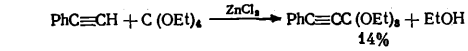
Acetylene reacts with ethyl orthoformate in the presence of zinc halides [88,89], the main reaction product being the tetraethylacetal of acetylenedialdehyde (XXI)—the tetraacetal of malonic dialdehyde (XXII) is formed as a side product:



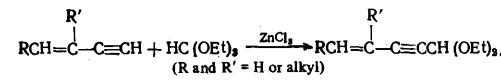
The reaction is of general validity. Alkyl- and arylacetylenes react with ethyl orthoformate, ethyl orthoacetate, and ethyl orthovalerate to form the diethylacetals of the corresponding acetylenic aldehydes and ketones:



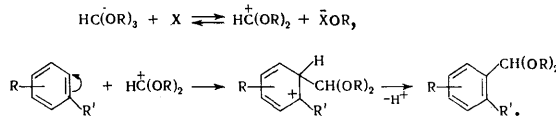
Highest yields (up to 80%) are achieved when ethyl formates are employed. In the reaction involving the orthoesters of alkanecarboxylic acids, the yields decrease approximately by a factor of two. Ethyl orthocarbonate gives rise to acetylenic orthoesters in low yields, for example:



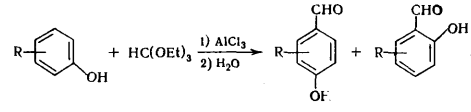
Substituted vinylacetylenes also enter into the reaction with ethyl orthoformate [90]:



The group of reactions including the interaction of dialkoxycarbonium ions with benzenoid of heterocyclic systems is of very great interest. They proceed via a general mechanism involving electrophilic substitution of an aromatic compound:

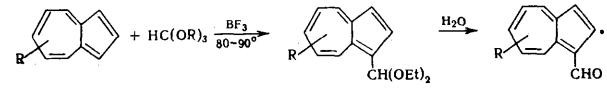


A new method of formylating phenols by orthoformic ester in the presence of aluminium chloride was proposed in 1963: [91]

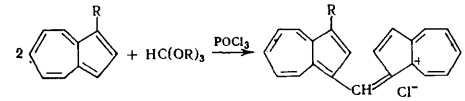


The method was tested on a large series of phenols, methylphenols, and naphthols [92]. Owing to its simplicity, it has substantial advantages over the methods of formylating the above compounds employed previously.

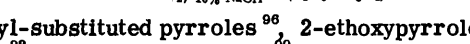
In the presence of acid catalysts (BF_3, $AlCl_3$, $SnCl_4$), azulene and its alkyl-substituted derivatives react with alkyl orthoformates to form the corresponding derivatives of azulene-3-aldehyde [93]:



In the presence of $POCl_3$, the interaction of ethyl orthoformate or ethyl thio-orthoformate with azulenes leads to azulenemonomethine dyes [94]:



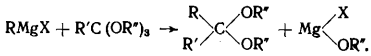
When ferrocene is treated with an excess of orthoester in the presence of $AlCl_3$, the following reaction takes place [95]:



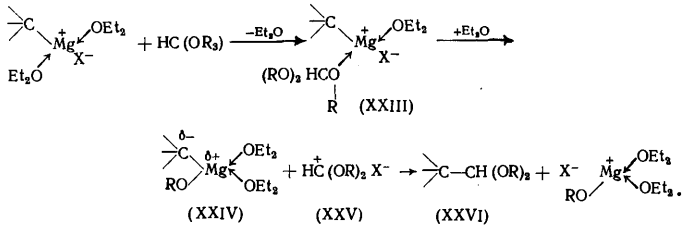
Alkyl-substituted pyrroles [96], 2-ethoxypyrroles [97], indoles [98], and 2-ethoxyindoles [99] react with ethyl orthoformate in the presence of acids (HCl, HBr, BF_3) to form monomethine derivatives.

VII. REACTIONS WITH ORGANOMETALLIC COMPOUNDS

Orthoesters react with organometallic compounds as follows:



Orthoformates give rise to acetals and the esters of other orthocarboxylic acids form ketals. In the reaction with orthocarbonic esters, the reaction products are other orthocarbonic esters. Probably the first reaction stage involves the formation of a coordination complex (XXIII) of the organometallic compound with the orthoester as a result of the replacement of a solvent molecule [1,100]. Subsequently the complex decomposes into the alkoxylated organometallic compound (XXIV) and the dialkoxycarbonium salt (XXV). Interaction between these intermediates yields the acetal (XXVI):



An organomagnesium compound plays the role of an acid activator of the orthoester in this reaction.

The method of acylation with orthoesters described above was proposed by Chichibabin [101]. The synthesis is carried out by refluxing a 1 : 1 mixture of components in ether or in higher-boiling solvents. For the reaction to be successful, it is sometimes necessary to evaporate the solvent after the addition of the orthoester to the solution of the organometallic compound. Frequently, instead of the acetals themselves, one isolates the corresponding aldehydes and ketones by hydrolysing the reaction mixture. The reaction may not stop at the acetal formation stage, since under certain conditions the latter are also capable of exchanging an alkoxy-group for an organic substituent of the organometallic compounds. Methyleneacetals and acetals of aliphatic aldehydes react with greater difficulty, aromatic aldehydes react more readily, and the reaction involving ketals is easiest [3]. In certain cases, all the alkoxy-groups of the orthoesters may be replaced, which results in the formation of a hydrocarbon [102].

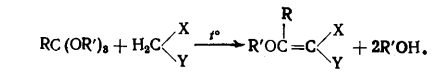
The first alkoxy-group is replaced most readily, the reaction being exothermic. The replacement of the second and even more so the third alkoxy-group requires an elevated temperature.

Aliphatic organometallic compounds form acetals in lower yields than aromatic derivatives. The yields of aliphatic acetals decrease with increase of the aliphatic chain length. Orthoformates are more reactive in this process than the orthoesters of alkenecarboxylic acid. In general, the method is convenient for the synthesis of aliphatic [1,103], aliphatic-aromatic [104], unsaturated [105], acetylenic [106], aromatic [107], and heterocyclic [108] aldehydes and ketones. More detailed information about this reaction and its conditions has been given in two monographs [1, 109].

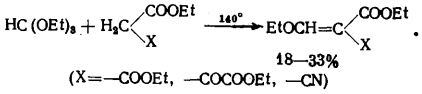
VIII. REACTIONS OF ORTHOESTERS WITH SUBSTANCES CONTAINING AN ACTIVE METHYLENE GROUP

1. Interaction of Orthoesters with Aliphatic Methylene Derivatives

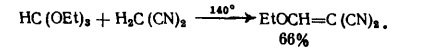
Orthoesters react with compounds containing an active methylene group via the mechanism



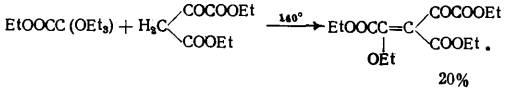
The substituents X and Y must be electronegative (COOR, COR, C≡N, and NO_2) and may be the same or of different types. The reaction proceeds on heating (140–150°C) the methylene derivatives with a small excess of the orthoester. The interactions of ethyl orthoformate with acetoacetic, oxaloacetic, and cyanocetic esters have been described [110]:



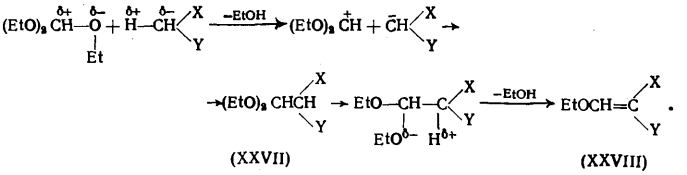
Ethyl orthoformate [110] and ethyl orthoacetate [111] show the greatest reactivity in this reaction (with malononitrile) forming the corresponding ethoxymethylene derivatives in high yields:



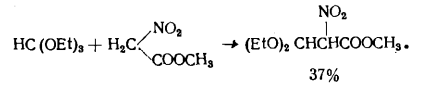
Triethoxyethyl acetate reacts with oxaloacetic ester [110]:



Post and Erickson [112] and also Jones [110] believe that the elimination of an alcohol from the orthoester must be preceded by additional polarisation of the C–O bond in the orthoester under the influence of the acidic hydrogen atoms of the methylene compound. One cannot rule out the possibility that at certain stages the reaction is ionic:



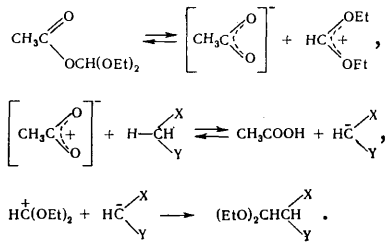
In certain cases, the intermediate acetal (XXVII) was isolated as the final reaction product. Thus, on heating ethyl nitroacetate with a small excess of ethyl orthoformate, the diethylacetal of methoxycarbonylnitroacetaldehyde is formed [113]:



When the acetal is heated to 170°C, a second alcohol molecule is split off and an ethoxymethylene derivative (XXVIII) (X = NO_2; Y = COOEt) is formed.

The diethylacetal of 2,2-dinitropropionaldehyde was synthesised similarly in 18% yield. Owing to the low yields of alkoxymethylene compounds, this method has little preparative value. A version of the synthesis first proposed by Claisen [114] and giving excellent results is employed in laboratory practice for the synthesis of alkoxymethylene compounds. In this procedure, a mixture of the orthoester and the methylene compound is refluxed in the presence of an excess of acetic anhydride which behaves as an activator of the orthoester, forming the reactive diethoxymethyl acetate and, moreover, shifts the reaction in the required direction by combining with the alcohol split off from the orthoester.

The higher reactivity of diethoxymethyl acetate in this reaction compared with ethyl orthoformate is due to the fact that the acetate anion is more stable than the alkoxide anion. Therefore diethoxy methyl acetate should undergo thermal dissociation to a considerable degree and the resulting acetate anion can deprotonate the methylene group:



Jones [115], who carefully separated all the products of the reaction of ethyl orthoformate with oxaloacetic ester in acetic anhydride and who determined their amount, proposed a mechanism involving successive transformations which accounts for all the compounds isolated (ethyl acetate, ethyl formate, acetic acid, and exothymethyleneoxaloacetic ester). The quantitative proportions of products which he found are in good agreement with the proportions calculated according to the mechanism proposed:

$$HC(OEt)_3 + (CH_3CO)_2O \rightarrow CH_3COOCH(OEt)_2 + CH_3COOEt,$$

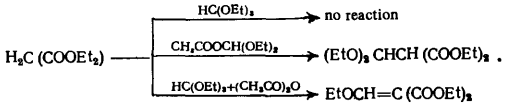
$$CH_3COOCH(OEt)_2 + H_2C(X)(Y) \rightarrow CH_3COOH + (EtO)_2CH-CH(X)(Y), \quad (XXIX)$$

$$(XXIX) \rightarrow EtOCH=C(X)(Y) + EtOH,$$

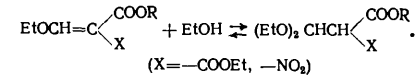
$$EtOH + (CH_3CO)_2O \rightarrow CH_3COOH + CH_3COOEt,$$

$$CH_3COOCH(OEt)_2 \xrightarrow{t^\circ} CH_3COOEt + HCOOEt.$$

Jones's mechanism also reflects two important factors which were already mentioned above. Firstly, the activating effect of acetic anhydride is shown only in the stage where the acetal (XXIX) is formed. Secondly, in the succeeding stage where the alcohol is split off by compound (XXIX) acetic anhydride serves only to bind the alcohol, displacing the reaction thereby to the right. These postulates are confirmed by the fact that diethyl malonate, a relatively inactive methylene compound, does not react with orthoesters in the absence of acetic anhydride [110] but does react with diethoxymethyl acetate to form only the acetal of formylmalonate [116], and ethoxymethylenemalonate is formed only on heating in the presence of an excess of acetic anhydride [117]:

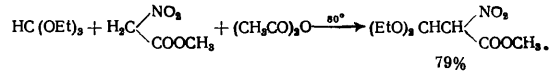


The assertion that acetic anhydride behaves as an alcohol-binding agent in the formation of the ethoxymethylene derivative from compound (XXIX) is consistent with the reversibility of this stage in the absence of acetic anhydride [116,118]:



(X=—COOEt, —NO_2)

It is also noteworthy that the acetic acid formed in the course of the reaction naturally catalyses the elimination of the alcohol from compound (XXIX). Under mild conditions, compound (XXIX) can be isolated even in the presence of acetic anhydride [118]:



The syntheses of ethoxymethylene derivatives in acetic anhydride from oxaloacetic ester, trifluoroacetic ester, ethyl acetylpyruvate [115], nitroacetic ester [119], acetylacetone [113], ethoxyacetylacetone [120], acetoacetic ester [113,121], ethyl acetonedicarboxylate [122], cyanoacetic ester [123,124], substituted amides of cyanoacetic acid [125,126], malononitrile [127,128], and benzoylacetic ester [129,130] have been described.

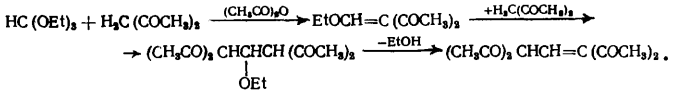
The reactivity of methylene compounds in reactions with orthoesters is higher the greater the electronegativity of the groups X and Y. The group C–N has the highest electronegativity, COR is less electronegative, and COOR is least electronegative.

The reaction with relatively unreactive methylene compounds requires catalysis. Thus prolonged refluxing in the presence of zinc chloride gives diethyl ethoxymethylenemalonate in high yield [131,132].

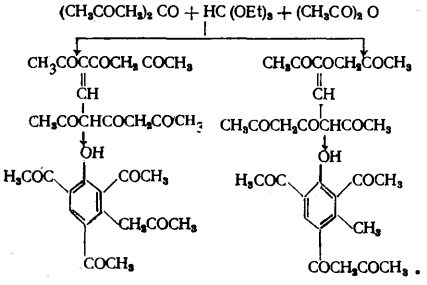
In view of the possibility of creating a system of conjugated bonds, it is possible to carry out the reaction of orthoformate esters with ethyl pyruvate [133]. The interaction of orthoesters with cyclopentene-1,3-dione [134] and indan-1,3-dione [135] has been described.

A patent has been taken out [136] for a method of synthesising alkoxymethylene compounds by the reaction of orthoesters with methylene derivatives in the presence of small amounts of glacial acetic acid as the catalyst with continuous distillation of the alcohol formed.

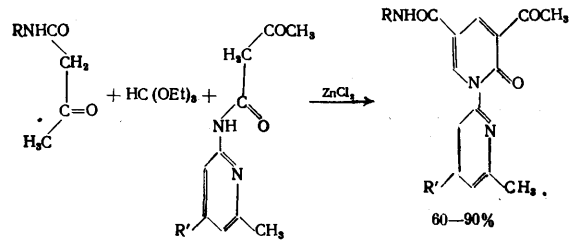
After prolonged heating of orthoesters with methylene compounds in acetic anhydride, one orthoester molecule condenses with two diketone or ketoester molecules [114]:



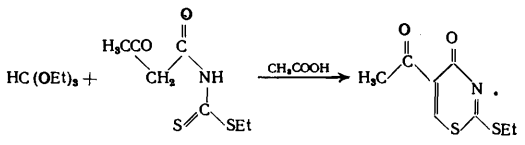
When diacetylacetone interacts with ethyl orthoformate in acetic anhydride, a mixture of isomers, cyclising under the reaction conditions into the corresponding phenols, is formed [137]:



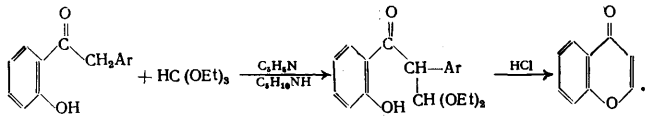
On refluxing in alcohol in the presence of $ZnCl_2$, cyclic products were obtained from substituted amides of acetoacetic acid [138]:



In the presence of a further reactive functional group in the molecule of the methylene derivative, internal cyclisation can occur [139]:

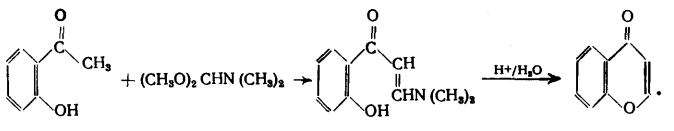


The methylene group in compounds containing a ketobenzyl group is also fairly reactive in the interaction with orthoesters in the presence of basic catalysts. A method of synthesising isoflavones by the condensation of orthoformate ester with benzyl *o*-hydroxyaryl ketones on heating in pyridine in the presence of piperidine was developed on this basis in 1949:[140]



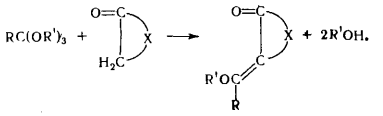
Subsequently the method found extensive application in the synthesis of a wide variety of natural isoflavones and their analogues, which are obtained in high yields.

A modification of the method has been used to synthesise chromone, the orthoester being replaced by the dimethylacetal of dimethylformamide, which functions simultaneously as a reactant and a basic catalyst [9]:

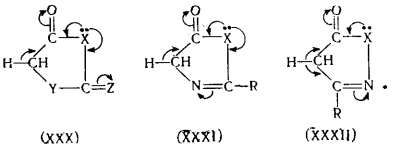


2. Condensation of Orthoesters with Heterocyclic Ketomethylene Compounds

Five- and six-membered ketomethylene compounds with one or two heteroatoms enter into the reaction with orthoesters. This results in the formation of heterocyclic alkoxyalkylidene derivatives:



A wide variety of five-membered heterocyclic systems, which enter into this reaction, correspond to one of the structures [135] presented below:



(XXX) (XXXI) (XXXII)

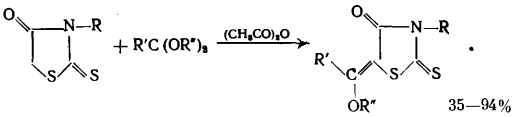
In the first two types [(XXX) and (XXXI)], the hydrogen atoms of the methylene group are activated mainly by the adjacent electronegative keto-group and to a considerable degree also by the fragment Y (XXX, Y = O, S, or NR) or $-N=C\langle$ (XXXI) owing to the $-I$ effect. The group X (O, S, or NR) lowers the electronegativity of the keto-group ($+M$ effect) and has a passivating influence on the methylene group. Passivation in structures (XXX) and (XXXI) is weakened by the influence of a second electronegative group (mesomeric with X) $-C=Z$ or $\rangle C=N-$.

In heterocyclic compounds of type (XXXII), the methylene group is activated simultaneously by the two highly electronegative fragments $-C=O$ and $-C=N$, which leads to a much higher reactivity of compounds of this type compared with (XXX) and (XXXI). Therefore, pyrazolones and isoxazolones (XXXII, X = N or O), for example, react readily with orthoesters in the absence of acetic anhydride, while compounds described by formulae (XXX) and (XXXI) have to be refluxed in acetic anhydride [135].

Steric factors are also important in the reactions of orthoesters, other than orthoformates, with ketomethylene compounds in which the atom adjoining the methylene group has a substituent. This effect can be demonstrated for 3-ethyl-2-thiothiazolidin-5-one, which condenses with ethyl orthoformate to form a planar 4-ethoxymethylene derivative, but does not react with ethyl orthoacetate. An analogous phenomenon has been observed for 1,3-disubstituted 2-thiohydantoins (XXX, X and Y = NR, Z = S) and other compounds with structure (XXX) and a bulky group Y.

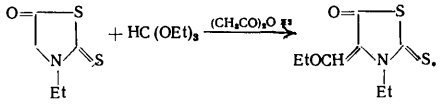
Pyrazolones (XXXII, X = NR) and isoxazolones (XXXII, X = O), which are more reactive, interact with ethyl orthoacetate and ethyl orthopropionate but the alkoxyalkylidene-derivatives formed are unstable for steric reasons. Ethyl thio-orthoformate cannot be made to react with the above types of ketomethylene compounds. Acetic anhydride plays the same role in this reaction as in the case of the acyclic methylene compounds discussed above.

A general method has been developed for the synthesis of 3-substituted 5,1′-alkoxyalkylidene-2-thionothiazolidin-4-ones by refluxing 3-R-rhodanine (R = aryl, alkyl, benzyl, cyclohexyl, allyl, and ethoxycarbonylmethyl) in the presence of an excess of orthoester and acetic anhydride [135,141,142]:

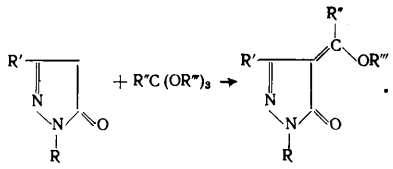


The highest yields of products are achieved with methyl and ethyl orthoacetates, while methyl and ethyl orthoformates and ethyl orthopropionate give somewhat less

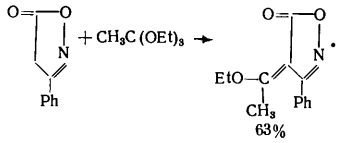
satisfactory results. When a mixture of 3-ethyl-2-thionothiazolidin-5-one is heated with ethyl orthoformate and acetic anhydride, the following reaction takes place [135]:



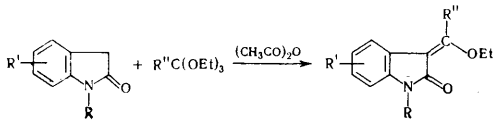
On refluxing with orthoesters in acetic anhydride [142] or in its absence [143], 1,3-disubstituted 5-pyrazolones readily form 4-alkoxyalkylidene derivatives:



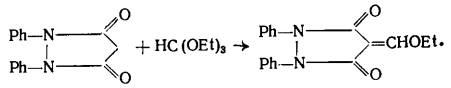
In the absence of acetic anhydride, 3-phenyloxazol-5-one reacts similarly with ethyl orthoacetate to form the unstable 4,1′-ethoxyethylidene-3-phenyloxazol-5-one [135]:



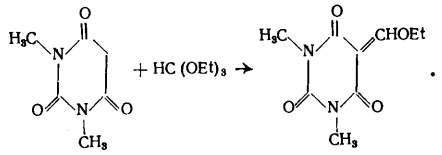
The condensation of orthoesters with oxindole [144] and its derivatives [145], in which the presence of a benzene ring causes additional activation of the methylene group, has been described:



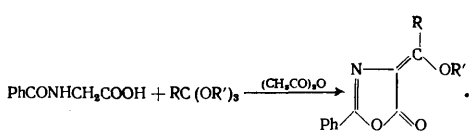
Diketomethylene heterocycles are also extremely reactive in the reaction with orthoesters. Ethyl orthoformate interacts with 1,2-diphenylpyrazole-3,5-dione [146]:



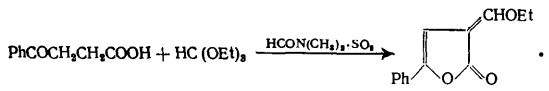
1,3-Dimethylbarbituric acid behaves similarly:



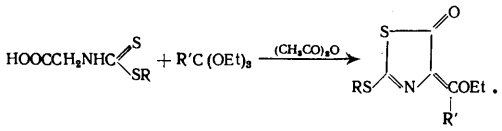
Frequently alkoxyalkylidene derivatives are synthesised in one stage from acyclic compounds. In such cases the condensation involving the methylene group is preceded by cyclisation with formation of a ketomethylene heterocycle. Thus, when hippuric acid was refluxed with orthoesters in acetic anhydride, 4,4′-alkoxyalkylidene-2-phenyloxazol-5-ones were obtained [147,148]:



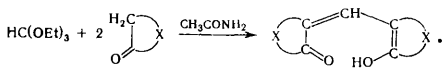
Benzoylpropionic acid reacts with ethyl orthoformate in the presence of a dimethylformamide–sulphur trioxide complex [149]:



N-(Ethylthiothionomethyl)glycine has been used [135] to synthesise 4,1′-alkoxyalkylidene-2-alkylthiothiazol-5-ones:

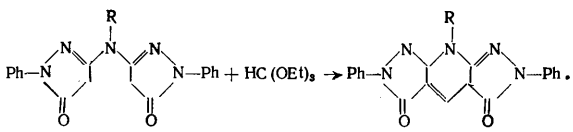


The reaction of orthoesters with ketomethylene heterocyclic compounds can lead to the so called oxonal dyes under certain conditions. Catalysis by a weak base (amides, pyridine) is sometimes used for such syntheses. Zenno [150] developed a method of synthesising oxonol dyes from ethyl orthoformate and certain ketomethylene heterocycles (3-methyl-1-phenylpyrazol-5-one, 3-ethylrhodanine, and barbituric, thiobarbituric, 1,3-diethylbarbituric, and 4-aminobarbituric acids) in the presence of acetamide:



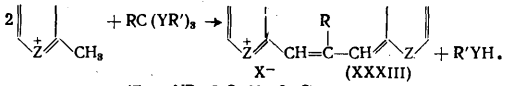
Oxonol dyes have also been obtained from 2-phenylthiazolidin-4-one [151] and certain 3-substituted 2-phenylpyrazolones [152].

The capacity of orthoesters to react with ketomethylene heterocycles can be used to cyclise certain compounds of suitable structure [153]:



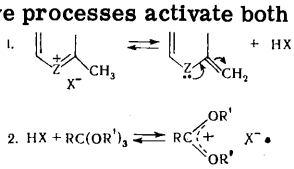
IX. SYNTHESES OF CYANINE DYES

Organic compounds containing a methyl group conjugated with a positively charged atom of a heterocyclic cation can react with orthoesters to form carbocyanine dyes (XXXIII):



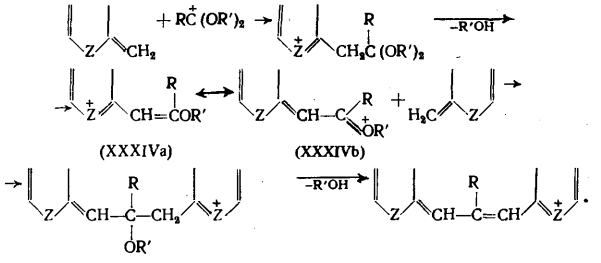
(Z=—NR, O,S; Y=O, S)

It is believed [154] that initially the charged system dissociates into a methylene base and an acid (HX), which reacts with the orthoesters to form a carboxonium salt. These consecutive processes activate both reactants:



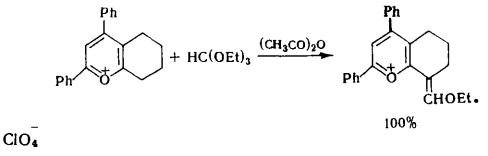
Dissociation is also promoted by solvents such as pyridine and acetic anhydride.

The aim of further reactions is clear from the following scheme:

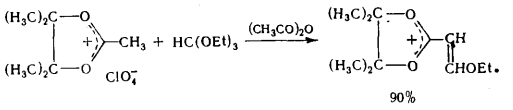


The scheme is valid also for thio-orthoesters.

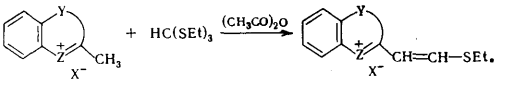
Mizuno and Tanabe [155] showed that the synthesis of cyanines does indeed proceed via an intermediate alkylidene derivative (XXXIV), which is also suggested by the sharp decrease of the yield of cyanine dyes in the presence of a large excess of orthoesters. In certain cases, alkoxyalkylidene compounds can be isolated as the main reaction product. Thus, when tetrahydrobenzopyrylium and tetrahydroxanthylium salts and their derivatives were heated briefly in acetic anhydride in the presence of ethyl orthoformate, the corresponding ethoxymethylene derivatives of these compounds were obtained [156,157]:



Ethoxymethylenedioxolanium salts are formed under similar conditions [158]:



This reaction is particularly characteristic of thio-orthoesters. For example, ethyl thio-orthoformate reacts with quaternary salts of 2-methylbenzothiazole, 2-methylbenzoxazole, and quinaldine on refluxing in acetic anhydride [159]:

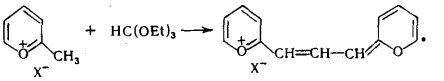


A wide variety of orthoesters are used in the synthesis of cyanine dyes. Orthoformates and thio-orthoformates form carbocyanines containing an unsubstituted trimethine chain (XXXIII, R = H) and orthoesters of higher acids give rise to dyes substituted at the central carbon atom of the chain. A wide variety of five-, six-, and seven-membered condensed systems condensed with other rings or charged monocyclic systems with one-, two-, or more heteroatoms can be involved in the reactions with orthoesters. Simple mononuclear heterocycles form cyanine dyes with greater difficulty than heterocycles condensed with aromatic rings.

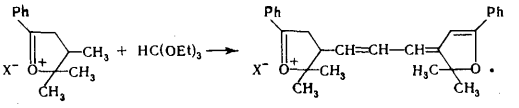
The greatest number of studies on the synthesis of cyanine dyes concern heterocycles of the thiazole series. Both monocyclic thiazolium salts [160] and salts condensed with benzene [161] and heterocyclic [162] rings have been used in the condensation reaction. The use of substituted imidazolium and benzimidazolium salts in this reaction has been described [163]. Pilyugin and coworkers synthesised cyanines from a wide variety of *N*-alkyl- and *N*-aryl-substituted quinaldinium [164] and benzoquinaldinium [165] quaternary salts. Lepidine derivatives [166] and other compounds containing the pyridine ring [167] enter into the reaction.

Trimethinecyanines are formed from benzoxazole [168], thienopyridine [169], 1,2,4-triazine [170], 1,4,7,9-tetra-azaindenes [171], 1,7-diazaindene [172], azepine [173], and tetrazole [174].

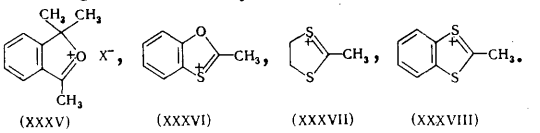
Oxonium heterocycles or their thio-analogues are used in the synthesis of cyanine dyes. Thus α- or γ-alkyl-substituted pyrylium [175] and benzopyrylium [176] salts and 9-methylxanthylium salts [177] readily form trimethine dyes on heating with ethyl orthoformate in pyridine or in a mixture of acetic anhydride and acetic acid:



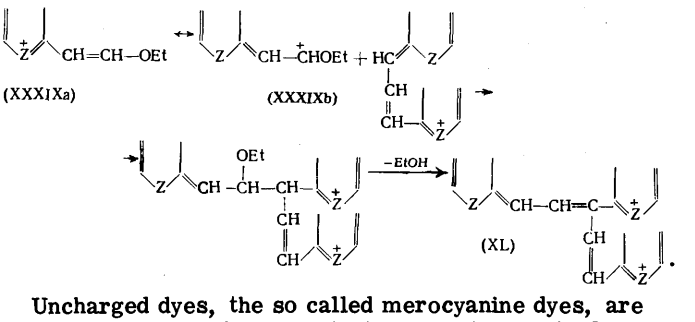
Non-aromatic furylium salts can also take part in the reaction [178]:



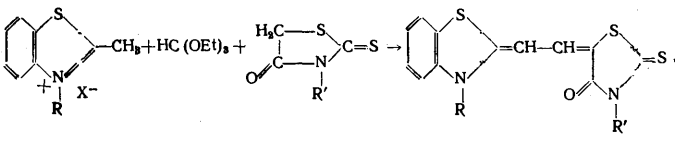
On heating in acetic acid or in a mixture of acetic anhydride and pyridine, ethyl orthoformate reacts with benzofurylium (XXXV) [179], benzoxanthylium (XXXVI) [180], dithiylium (XXXVII) [180] and benzodithiylium (XXXVIII) salts, forming trimethine dyes:



Trinuclear neocyanine dyes, for which Konig's formula (XL) [154] was recently shown to be correct [155], are almost invariably formed as side products in the synthesis of trimethinecyanines. The mechanism of the formation of neocyanines was investigated by Japanese workers [155], who observed that the yield of neocyanines is lower the higher the yield of trimethinecyanines. This indicates competition between two modes of binding of the alkoxymethylene cation (XXXIX):

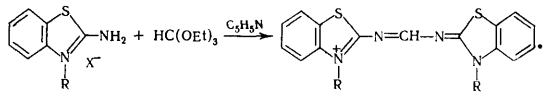


Uncharged dyes, the so called merocyanine dyes, are obtained when one of the reactants is a heterocyclic ketomethylene derivative and the other is a quaternary salt of a nitrogen-containing heterocycle [182]. For example:



Ethyl orthoformates react similarly with barbituric or thiobarbituric acid and quaternary salts of nitrogen-containing heterocycles (α-picoline, 2,6-lutidine, quinaldine, and 2-methylbenzothiazole)[183].

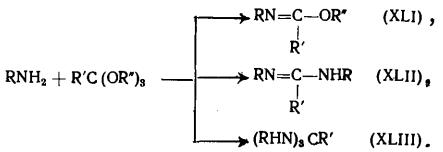
Orthoesters are suitable for the synthesis of azacyanines—compounds in which one or several methine groups are substituted by nitrogen atoms[184,185]:



X. REACTIONS OF ORTHOESTERS WITH AMINO-DERIVATIVES

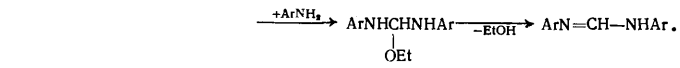
1. Synthesis of Acyclic Products

When orthoesters react with substances containing an amino-group (amines, amides, substituted ureas, and hydrazines, hydrazides, etc.) products of three types may be obtained depending on the reaction conditions and the structure and relative amounts of the components:



The first two reactions, which lead to imidoesters [imidates] (XLI) and amidines (XLII) respectively, are general, while the formation of nitrogenous analogues of orthoesters (XLIII) is possible only from certain compounds of suitable structure and constitutes a special case. Since the synthesis of imidoesters and amidines with the aid of orthoesters has been discussed in a number of reviews[186-188], we shall consider only the fundamental studies carried out recently.

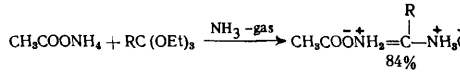
Spectroscopic studies on the reaction of aniline with ethyl orthoformate showed[189] that imidoesters are intermediates in the synthesis of amidines:



The formation of *N*-arylformimidoesters[51] becomes possible under the conditions of acid catalysis when the activation of orthoformate by the acid causes the rate of formation of the formimidoester to predominate over the rate of its conversion into diarylformamidine.

Roberts et al.[190] developed a general method for the synthesis of *N*-phenylformimidoesters by the reaction of alkyl orthoformate with aniline.

Ammonium acetate reacts with ethyl orthoformate and ethyl orthoacetate to form amidinium acetates[191]:

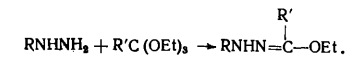


Dimethylformamidine is obtained by passing gaseous methylamine through ethyl orthoformate[192]. The synthesis of higher *NN*-dialkylformamidines in the presence of boron trifluoride-ether has also been described[193].

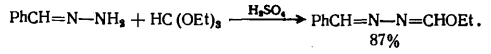
Heterocyclic bases react with orthoesters too. *N*-Heterocyclic derivatives of formimidoesters of the pyrazole[194], imidazole[194], isoxazole[195], isothiazole[196], and pyridine[197] series have been obtained.

Syntheses of formamidines from 5-aminopyrazole[198], 3-amino-2-pyrazoline[199], 2-aminopyrimidine[200], and 3-aminoisoxazole[201] have been described.

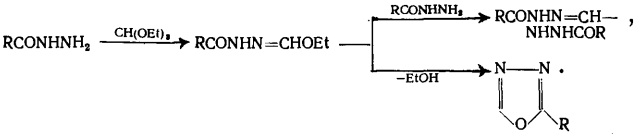
On heating with orthoesters, arylhydrazines[202] give high yields of ethoxyalkylidenehydrazines:



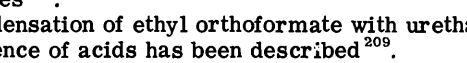
The reaction of benzaldehyde hydrazone with a fourfold excess of ethyl orthoformate in the presence of sulphuric acid yields ethoxymethylenephenylmethylenehydrazine, which contains conjugated double bonds[203]:



The reaction of carboxylic acid hydrazides with ethyl orthoformate, which can give rise to cyclic products in addition to ethoxymethylenehydrazides and hydrazidomethylenehydrazides takes place in a more complex manner[204,205]:



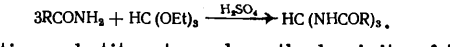
Owing to the reduced reactivity of the amino-group in acid amides, their reactivity in relation to orthoesters is much lower than that of amines, hydrazines, and hydrazides. Whereas ethyl orthoformate still reacts with acetamide and benzamide, giving low yields of diacylformamidines[206], ethyl orthoacetate can no longer be made to react in this way[207]:



The reactivity of urea and its derivatives is similar to that of acid amides. On refluxing with ethyl orthoformate, urea and its alkyl and arylalkyl derivatives yield high-melting sparingly soluble products—*NN*-dicarbamoylformamidines[208].

The condensation of ethyl orthoformate with urethanes in the presence of acids has been described[209].

The condensation of three moles of an amide with one mole of orthoester in boiling toluene yields triacylaminomethanes[210]:



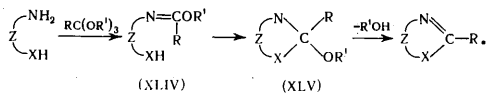
Electronegative substituents reduce the basicity of the amide and the yields of products are low.

2. Synthesis of Cyclic Compounds

When the molecule contains two amino-groups, the reaction usually leads to the formation of cyclic amidines. Cyclic systems with different heteroatoms are obtained when other functional groups are introduced into the reaction apart from the amino-group. The cyclisation is achieved by heating the components with or without the distillation of the alcohol.

It was sometimes possible to isolate the intermediates (XLIV) and (XLV) in the cyclisation reaction. The elimination of the alcohol from the alkoxy-derivative

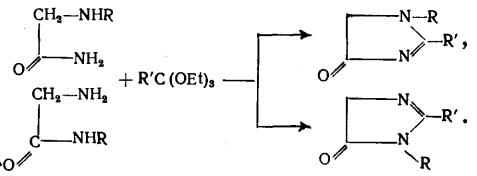
(XLV) is the rate-determining stage of the cyclisation process:



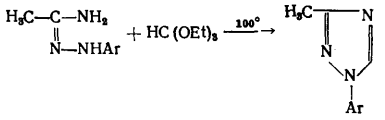
(XLIV) (XLV)

Usually X is a substituted or a free amino-group, oxygen, or sulphur. The group Z can be a carbochain or heterochain bridge and also constitutes part of a carbocyclic or heterocyclic system.

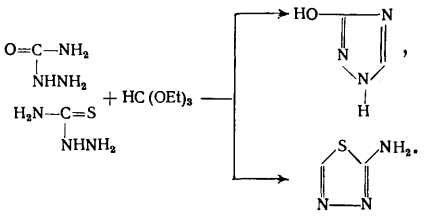
A general method of synthesising 4-imidazolones and 5-imidazalones is based on the cyclisation of *N*- or *N'*-substituted glycine amides [211]:



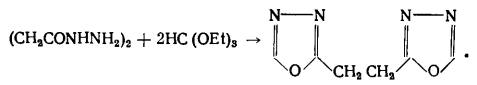
Acetamide arylhydrazones react with ethyl orthoformate to form 1-aryl-3-methyl-1,2,4-triazoles [212]:



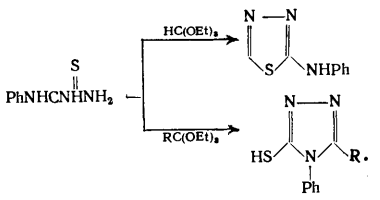
It is interesting that semicarbazide [213] and thiosemicarbazide [214] hydrochlorides form different types of heterocycles:



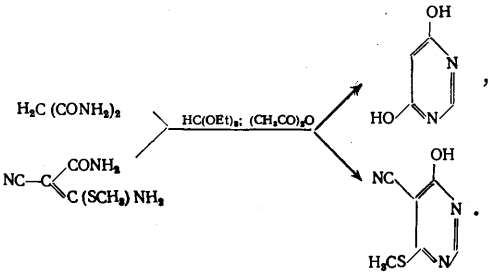
The synthesis [215] of heterodiazoles on refluxing hydrazides and thiohydrazides of alkyl- and aryl-substituted and heterocyclic carboxylic acids with orthoesters has been described. Succinic acid dihydrazide undergoes biscyclisation on treatment with ethyl orthoformate [204]:



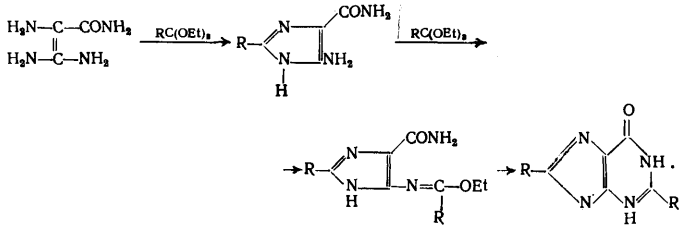
Owing to differences in the reactivities of orthoformates, the reaction of 4-phenylthiosemicarbazide with ethyl orthoformate or the orthoesters of alkanecarboxylic acids (ethyl orthoacetate and ethyl orthopropionate) gives two types of heterocycles[216]:



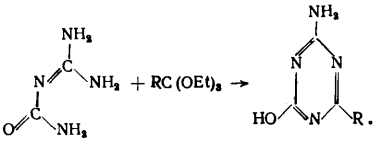
Malonodiamide [213] and 3-amino-2-cyano-3-methylthioacrylic acid cyclise in the presence of acetic anhydride [217]:



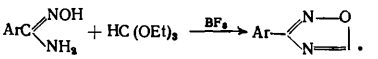
Hypoxanthine[218] and a number of its substituted derivatives [219] are obtained under similar conditions. The reaction proceeds via the formation of intermediates, which have been isolated:



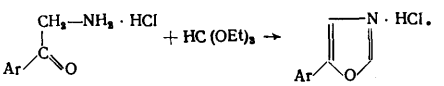
Guanylurea [220] can be condensed with orthoesters and the dimethylacetal of dimethylformamide with formation of substituted 1,3,5-triazines:



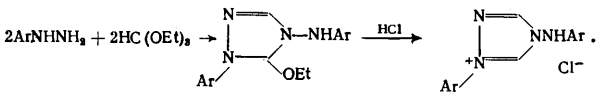
A convenient method for the synthesis of 3-aryl-1,2,4-oxadiazoles consists in heating the amidoximes of arylcarboxylic acids with ethyl orthoformate in the presence of boron trifluoride-ether [221]:



Oxazoles can be prepared from the hydrochlorides of substituted ω-aminoacetophenones and ethyl orthoformate [222]:

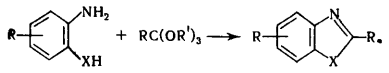


Arylhydrazines with electron-donating substituents in the benzene ring yield derivatives of 1,2,4-triazole on interaction with ethyl orthoformate [202]:



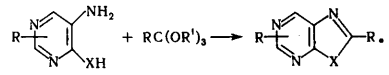
Condensed heterocyclic systems can be synthesised when the functional groups involved in cyclisation occupy the 1- and 2-positions in the benzene or heterocyclic ring.

When ring-substituted *o*-phenylenediamines[223], *o*-aminophenols[224], and *o*-aminothiophenols[225] react with orthoesters, the products are derivatives of benzimidazole, benzoxazole, and benzothiazole respectively:

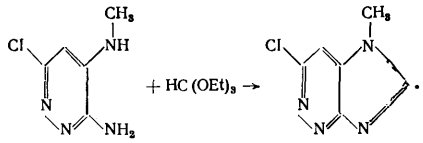


(X = NH; O; S; NR)

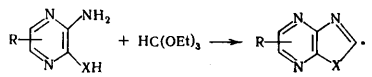
Heterocyclic compounds containing purine and thiazolopyrimidine groups were synthesised similarly from a wide variety of derivatives of 4,5-diamino,[226] 4-R-amino-5-amino-[227], and 5-amino-4-mercapto-pyrimidines[228]:



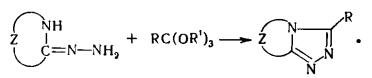
A substituted imidazopyridazine is obtained when 3-amino-6-chloro-4-methylaminopyridazine is heated with ethyl orthoformate[229]:



Syntheses of imidazopyrazines have been described[216,230]



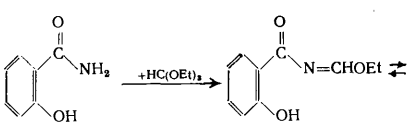
Heterocyclic systems containing three nitrogen atoms in the ring are formed when the hydrazones of a wide variety of heterocyclic keto-derivatives react with orthoesters:



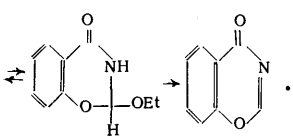
The hydrazones of 2-benzimidazolone, 2-benzoselenazolone[216], 2-quinolone[216], derivatives of 2-pyrimidinone[231], 4-quinazolone[232], 2-quinoxalinone[233], and imidazopyridazinone[234] can participate in this reaction.

When the amides of aromatic or heterocyclic carboxylic acids containing an active functional group in the *ortho*-position are introduced into the reaction with orthoesters, the products are six-membered heterocyclic keto-derivatives with two heteroatoms in the ring.

When the amide of salicyclic acid was refluxed with ethyl orthoformate, an intermediate iminoether (XLVI), which is a tautomer of the cyclic product (XLVII), was isolated[213,235]:



(XLVI)

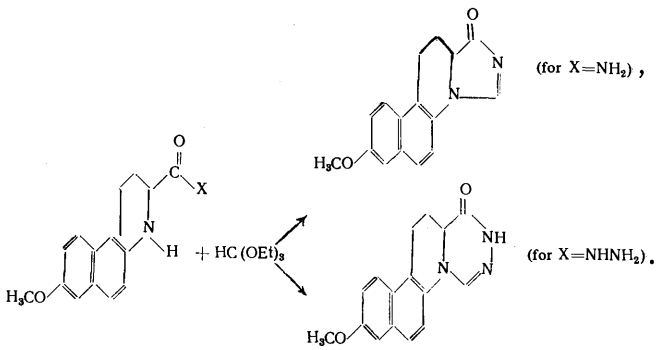


(XLVII)

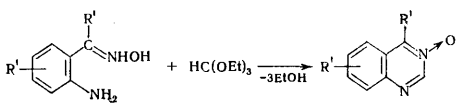
The reaction of the amide of anthranilic acid with ethyl orthoformate gives 4-quinazolone[213].

Apart from the amides of aromatic acid, a wide variety of heterocyclic *o*-substituted carbamides are used for similar cyclisations. The use of imidazole[236], isoxazole[237], 1,2,3-triazole[238], quinoline[239], pyrimidine[240], and pyrazine[241] derivatives has been described.

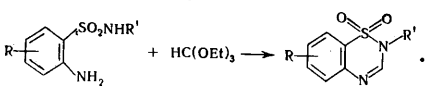
This principle has also been employed to synthesise di- and tri-azasteroid systems[242]:



On being refluxed with an excess of ethyl orthoformate, *o*-amino-derivatives of aldoximes and ketoximes give rise to quinazoline $N_{(3)}$-oxides[243]:

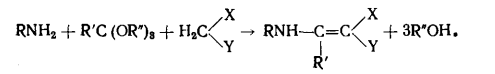


Aromatic sulphonamides with *o*-amino-substituents react with *o*-aminocarbamides, the difference being that in this case *SS*-dioxide rings are formed[244]:

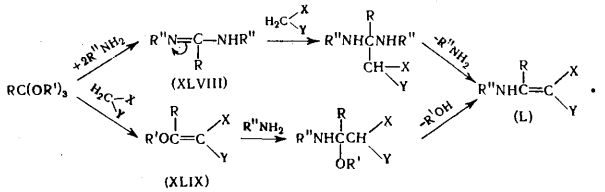


XI. THREE-COMPONENT CONDENSATIONS

This group combines single-stage reactions of orthoesters with amino-compounds (arylamines, heterocyclic amines, urea, and substituted ureas) and substances which can react as CH acids. For example:

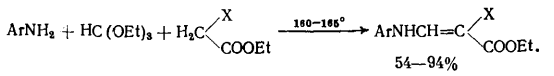


At first sight this reaction resembles the Mannich reaction. The difference is that the Mannich reaction gives rise to a monofunctional aminoalkyl group $\rangle N-\overset{|}{C}-\overset{|}{C}-$, while the use of orthoesters yields the bifunctional enamine unit $\rangle N-\overset{|}{C}=\overset{|}{C}-$. Probably the reaction proceeds simultaneously via two similar mechanisms:

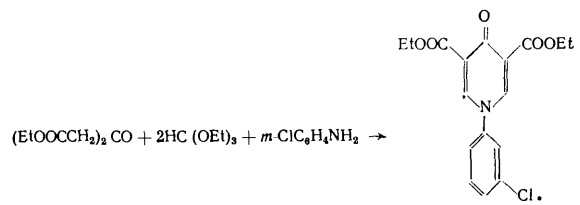


The yields of the intermediates (XLVIII) and (XLIX), where these are obtained specially by heating the components in pairs (the amine and the orthoester or the CH acid and the orthoester) are frequently much lower than the yield of the final product (L) obtained when all three starting materials are involved simultaneously in the reaction. Evidently the reason for this phenomenon may consist in a favourable mutual influence of the starting materials on one another. On the one hand, the formation of the alkoxyalkylidene compound (XLIX) should undoubtedly be facilitated by the catalytic action of the base (amine), while the acidity of the methylene component is a factor promoting the activation of the orthoester and therefore facilitating both reactions. Moreover, the products of the interaction of any pair of the starting compounds are removed from the sphere of the reversible reaction owing to the interaction with the third component.

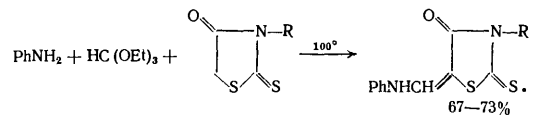
Three-component condensation was achieved for the first time by Snyder and Jones [244], who developed a method for synthesising β-arylamino-substituted acrylic esters by the reaction of compounds containing an active methylene group with aromatic amines and ethyl orthoformate:



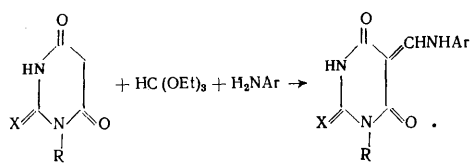
Later a general method was developed for the synthesis of a wide variety of enamines by the reaction of orthoesters with compounds containing an active methylene group and with arylamines [245]. The reaction of acetonedicarboxylic acid esters with ethyl orthoformate and *m*-chloroaniline gives a substituted pyridone [244]:



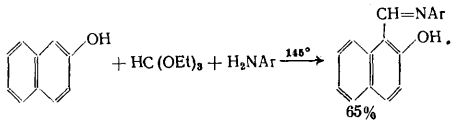
Ketomethylene heterocyclic derivatives may serve as the CH acid components in the reaction with aromatic amines and ethyl orthoformate [246]:



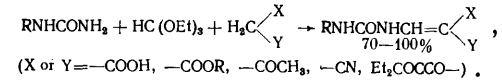
On heating with ethyl orthoformate and aromatic amines, barbituric [247], thiobarbituric [247], and 1,3-dimethylbarbituric [248] acids form arylaminomethylenebarbiturates:



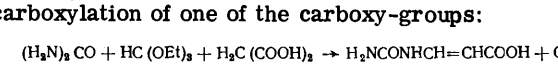
Aromatic phenolic systems can also behave as the CH acid components [249]. In this case the products are not enamines but Schiff bases:



Apart from aromatic amines, substituted ureas participate in this reaction. Whitehead [250,251] developed a general method for synthesising ureidoethylenes by the reaction of ethyl orthoformate with urea, *N*-cyclohexylurea, *N*-alkylureas, and *N*-arylalkylureas and compounds containing an active methylene group:

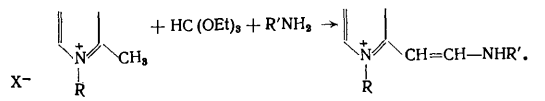


It was shown that the activity of the methylene component in this reaction decreases in the sequence COOH > CN > > $COCH_3 \gg COOC_2H_5$. Malonic acid and oxaloacetic ester, which are the most reactive, react even at room temperature; the reactions with acetylacetone, cyanoacetamide, acetoacetic ester, and cyanoacetic ester require heating for 8–12 h, while in the case of malononitrile refluxing for 1–2 h is sufficient. When malonic acid is allowed to react with ethyl orthoformate and urea on heating, the condensation involves the simultaneous decarboxylation of one of the carboxy-groups:

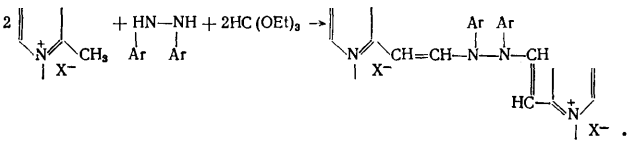


Other examples of the reaction of ethyl orthoformate with urea [252] or alkylureas [253–255] and cyanoacetic ester [256], malononitrile [255,257], nitroacetic ester [258], α-nitroacetonitrile [254], oxaloacetic ester [252], acetylpyruvate [252] and acetylacetothienone [259] have also been described.

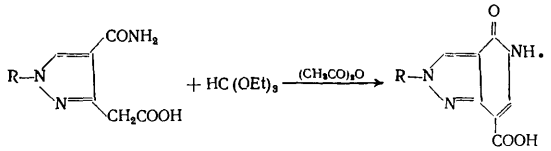
Knott [260] and Dzenno [261] showed that methyl-substituted quaternary salts of nitrogen-containing heterocycles (α-picoline, 2,6-lutidine, quinaldine, and 2-methylbenzothiazole) can take part in the reaction with ethyl orthoformate and aromatic amines (aniline, toluidine, *m*-aminophenol, *p*-aminoacetophenone):



Symmetrical disubstituted hydrazines, benzidine, and certain other diamines form bisdiaminodivinyl derivatives [262]:



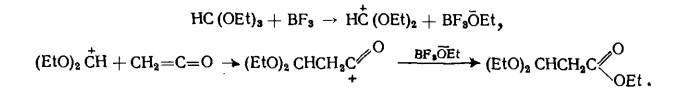
When the molecule contains an amino- and an active methylene group simultaneously, internal condensation with formation of a cyclic product takes place [263]:



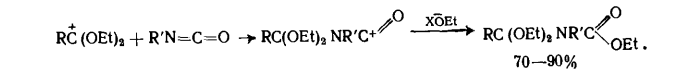
XII. OTHER REACTIONS OF ORTHOESTERS

The reactions of orthoesters with individual compounds, which do not fit the classification adopted in the review, are considered in this section.

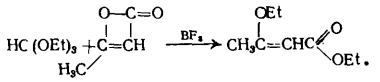
In the presence of zinc chloride or boron trifluoride, ethyl orthoformate reacts with keten [264,265] according to the following mechanism:



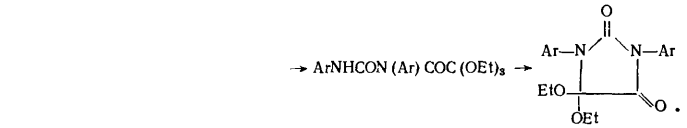
The interaction of orthoesters on heating with aliphatic, alicyclic, and aromatic isocyanates and also with polyisocyanates in the presence of acidic condensing agents (BF_3, $ZnCl_2$, $AlCl_3$) involves a similar mechanism [266,267]:



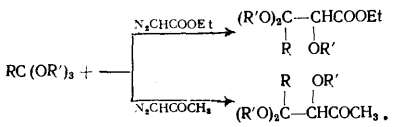
Acid catalysis is also essential for the reaction of ethyl orthoformate with diketen [77]:



In the absence of acids, the reaction of isocyanates with orthoesters proceeds via a different mechanism. Thus Whitehead and Traverso [268] found that, when aryl isocyanates are refluxed (for 12–24 h) in the presence of an excess of ethyl orthoformate, 1,3-diaryl-5,5-diethoxyhydantoins are formed:

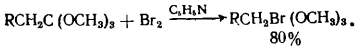


In the presence of Lewis acids, diazoacetic ester and diazoacetone react with orthoesters to form addition products [269]:

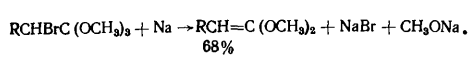


The reaction proceeds with evolution of nitrogen and the yields of products are 37–99%.

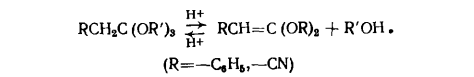
The α-methylene group of the orthoesters of alkanecarboxylic acids [270] and phenylacetic acid [271] is readily brominated, the other groups remaining unaffected:



The bromo-derivatives of orthoesters can be used to prepare keten acetals [270]:

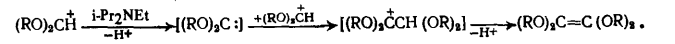


Orthoesters containing in the α-position an activating group, such as phenyl [271] or the cyano-group [272], are a convenient source from which keten acetals may be obtained. In this case the alcohol may be split off both as a result of pyrolysis at 220–230°C and under the conditions of acid catalysis, the reaction being reversible in the presence of acids:

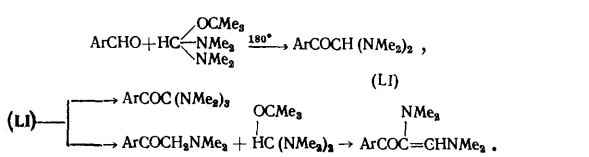


In certain cases, catalysis by strong bases was employed in the synthesis of keten acetals from orthoesters [273].

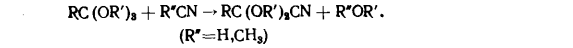
The formation of carbenes on treatment of di(methylthio)- or dialkoxy-carbonium salts of ethyldi-isopropylamine in methylene chloride at −10°C was reported recently [274]. The carbene dimerises under the reaction conditions, forming tetrasubstituted ethylenes:



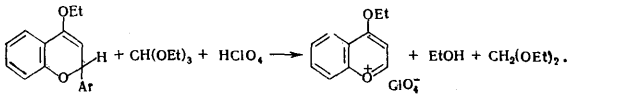
The interaction of aromatic aldehydes with nitrogenous analogues of orthoesters is unusual [275]. The aminal of arylglyoxal (LI) formed initially subsequently disproportionates via the Cannizzaro reaction:



The interaction of hydrocyanic acid [276] and acetonitrile [277] with orthoesters leads to the replacement of the alkoxy-group by a cyano-group:



In the presence of acidic agents, orthoesters can behave as hydride ion acceptors [278]:



The examples quoted in the present review by no means exhaust all the applications of orthoesters in organic synthesis.

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Institute of Physical and
Organic Chemistry at
Rostov-on-Don State
University

U.D.C. 547.307

Advances in the Synthesis of Purine Derivatives from Uric Acid

E.S.Golovchinskaya

The review deals mainly with the discussion of the synthesis of purine derivatives based on the interaction between uric acid and acetic anhydride. Problems of the structure, intermediates in the reaction, *N*-methylated derivatives of the compounds, and their conversion into 8-methylxanthines are discussed. Much attention has been devoted to the synthesis of 9-methylpurine derivatives from uric acid using 1,3,8,9-tetramethylxanthine as an intermediate. Various methods of synthesising *N*-methylated purines substituted in the 8-position have been described.
The bibliography includes 157 references.

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I. INTRODUCTION

In the course of the last two decades, synthetic studies on purines have developed on an enormous scale throughout the world. The great interest in purine derivatives, which re-emerged in the 1950's after a fairly long slack period, has been to a great extent the result of the outstanding advances achieved in the study of various enzymes systems, cell biochemistry, and principally the structure and role of nucleic acids. This renewed interest is associated with one of the most urgent problems in modern medicine—the search for effective therapeutic agents for the treatment of diseases involving various types of impairment of nucleic acid metabolism, including those used in the fight against malignant diseases. Numerous studies in this field ultimately led to the synthesis of many hundreds of new derivatives of purine and its analogues, the aim being to investigate their biological activity.

All the syntheses in the purine series described in the literature may be divided into two groups. The first and largest group includes methods based on successive or simultaneous synthesis of the pyrimidine and imidazole rings of the purine molecule[1-3]. A fairly exhaustive systematic account of these methods has been given in a number of reviews (including Robins's detailed review[4]) and they will not be considered in this paper.

The syntheses of the second group, based on the so called semisynthetic methods, i.e. on the employment and reactions of natural compounds already containing a purine skeleton, have been much less satisfactorily described in the review literature.

More than 30 natural purines from various sources of plant and animal origin are known. These are primarily the aglucones of nucleosides constituting the structural elements of nucleic acids, the purine components of antibiotics (puromycin, nebularine, etc.), and also the normal metabolic products of the organisms of higher animals. Despite the comparatively great variety of the purine glucosides known at present, the fairly constant structure of their purine moiety is striking—with rare exceptions this is adenine and its derivatives substituted at the amino-group or at $C_{(2)}$ and also guanine and its derivatives methylated at the exocyclic nitrogen atom or at the $N_{(1)}$ atom.[5]

Recently a substance called herbipoline, characterised as a new type of purine derivatives, mainly purinium betaines with a zwitter-ionic structure hitherto unknown for purine, was recently isolated from the organisms of lower animals, in particular from the stroma of the sponge *Geodia gigas*[6,7]. Natural 1-methyladenine, identified by comparison with the synthetic specimen and called by the author spongopurine, was obtained from the same source[8].

With the exception of the main examples of aglucones mentioned above—adenine and guanine—almost inexhaustible amounts of which are available in living organisms, the remaining aminopurines are present in the organs and tissues of animals in very small amounts and their isolation and characterisation constitute refined and laborious operations. From this standpoint, the most promising natural purines are uric acid and two purine alkaloids from the group of methylated xanthines—caffeine and theobromine. The amounts of these purine derivatives in nature are fairly large and methods for their extraction from natural sources on an industrial scale have been developed.

Uric acid is the final product of the protein metabolism of birds and reptiles and is present in large amounts in the excrement of these animals. The guano deposits, from which it is derived, have now become appreciably depleted. During the Second World War, industrial manufacture of uric acid, based on the extraction of chicken dung diluted with alkali, which contains 2–3% (relative to the dry material) of uric acid, was organised in the Soviet Union in state poultry farms. The uric acid obtained in this way served as the raw material for the synthesis of caffeine and theophylline as well as methylcaffeine; the last derivative was manufactured for several years as an independent preparation which successfully replaced caffeine in several cases[9].

This review deals with the syntheses of purines based on the reactions of uric acid. It includes also studies on the synthesis of purine derivatives from caffeine and theobromine, which are logically related to the synthesis of the same compounds from uric acids.

II. REACTIONS OF URIC ACID

Practically all known reactions of uric acid(I) which result in the derivatives of di- and monoxopurines (including xanthine and hypoxanthine), as well as oxygen-free purines can be classified into three types of reactions.

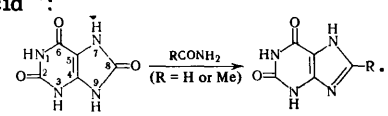
1. Interaction with Phosphoryl Chloride and Subsequent Reactions of the Resulting 2,6,8-Trichloropurine.

This series of reactions, already described by Fischer in the past century, permitted a reliable determination of the structure of uric acid and also the structures of natural purines already known at the time, such as adenine hypoxanthine, guanine, and others. The synthesis of trichloropurine and its reactions confirmed the structural relations between these natural purines and uric acid and with one another, culminated in the synthesis of the parent compound of this class (unsubstituted purine), and served as a firm foundation for a detailed elucidation of the chemistry of purines[10].

The scientific value of the brilliant studies by Fischer has persisted until the present day but the reaction between uric acid and phosphoryl chloride has been very rarely employed for preparative purposes.

2. Direct Conversion into Xanthines by Refluxing with Formamide (or Other Amides)

This completely new reaction, discovered by Bredereck and coworkers, can serve according to the authors as a quite realistic basis for a two-stage synthesis of caffeine from uric acid[11]:



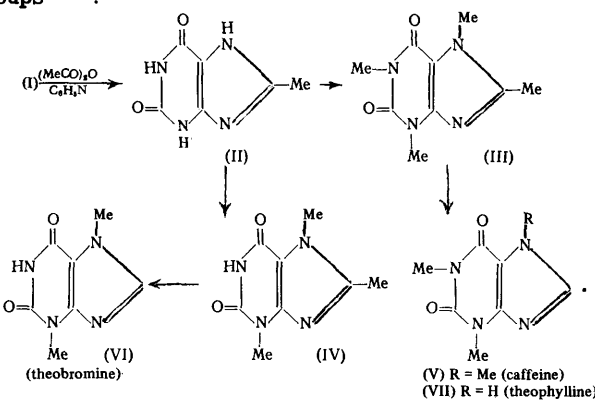
(I)

The authors convincingly disproved the possibility that the essential feature of the process is reduction by formamide of the $>C_{(8)}=O$ ($>C_{(8)}$–OH) fragment of the imidazolone ring. On the basis of the formation of 8-methylxanthine in a similar reaction with acetamide and also of a number of experimental data, they believe that, on heating with formamide, the imidazolone ring of uric acid is cleaved; this is accompanied by a reaction of the resulting 5-formylamino-4-ureidouracil culminating in ring closure. The authors assert that the precursor of the $C_{(8)}$ atom of the imidazole ring in the resulting xanthine is not the $C_{(8)}$ atom of the initial uric acid but the carbon atom of formamide.

The observation that on heating with formamide in an autoclave uric acid can be converted not only into xanthine but also into hypoxanthine is likewise noteworthy. The importance of this reaction, which has no preparative value, is due to the fact that it clearly indicates the capacity of the ureide group of both the imidazole and pyrimidine ring to react with formamide[12].

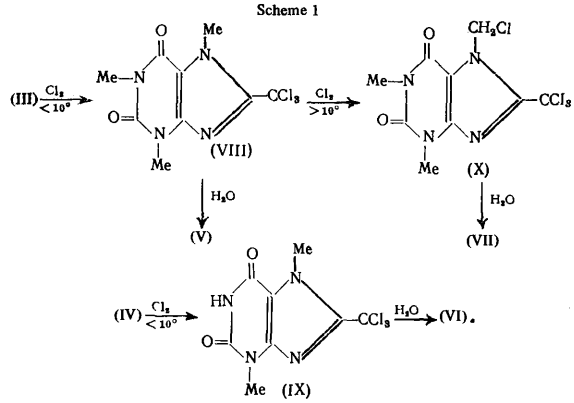
3. Interaction with Aliphatic Acid Anhydrides (Mainly Acetic Anhydride)

This reaction constitutes the basis of a whole group of patents taken out by the Boehringer Company which enabled a realistic synthesis of all three purine alkaloids (caffeine, theobromine, and theophylline) in a single common industrial scheme as early as the beginning of the present century. The first stage of this synthesis is the conversion of uric acid into 8-methylxanthine (II), which is formed in a nearly quantitative yield as a result of refluxing it for 80 h with an excess of acetic anhydride in the presence of pyridine or other pyridine bases[13]. Next, methylation of 8-methylxanthine leads to the formation of 8-methylcaffeine (III) or 8-methyltheobromine (IV) depending on the reaction conditions[14,15]. As a result of the removal of the methyl group from the $C_{(8)}$ atom in compounds (III) and (IV), caffeine (V) and theobromine (VI) are formed respectively[16,17]. In addition, methylcaffeine can be converted also into theophylline (VII) as a result of the simultaneous elimination of the $C_{(8)}$- and $N_{(7)}$-methyl groups[17,18]:



The removal of methyl groups from compounds (III) and (IV), i.e. their conversion into caffeine, theophylline, and theobromine, is achieved, in accordance with the above patents, by the substitution of hydrogen atoms in these groups by chlorine and subsequent hydrolytic removal of the chloromethyl groups from the resulting trichlorides (VIII) and (IX) and also from the tetrachloride (X)

Scheme 1

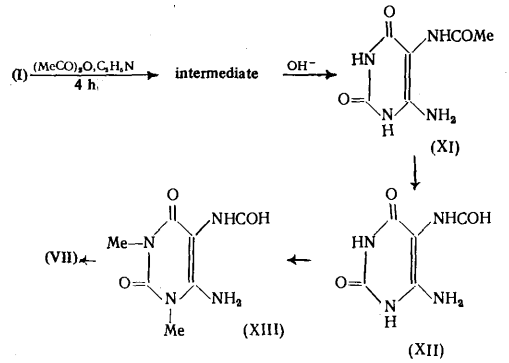


Scheme I has found wide-scale practical application and was used, in particular, in Soviet chemical-pharmaceutical industries in 1943–1953[19–29] for the synthesis of caffeine and theophylline.

Scheme 2 for the synthesis of theophylline, whereby it is also manufactured in the USSR, is based on the reaction between uric acid and acetic anhydride interrupted after a period of 4 h, the conversion of the resulting intermediate by hydrolysis into 5-acetamido-4-aminouracil (XI), and the transacylation of the latter by treatment with formic acid. 4-Amino-5-formamidouracil (XII) was methylated and the resulting 4-amino-5-formamido-1,3-dimethyluracil (XIII) was converted by cyclisation into theophylline (VII)[30–33] (Scheme 2).

Nowadays the industrial synthesis of purine alkaloids from uric acid has been displaced in many countries (and possibly throughout the world by economically more effective synthetic methods. Nevertheless the interaction of uric acid with acetic anhydride and also the substitution of hydrogen atoms in the methyl groups of *N*-methylated 8-methylxanthines by chlorine and subsequent hydrolytic

Scheme 2

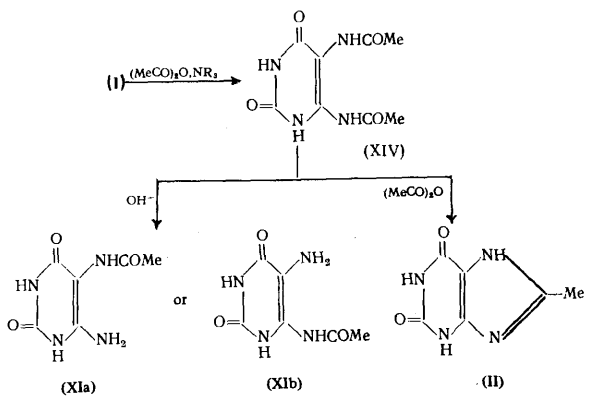


cleavage of the chloromethyl groups survived for a long time their "elimination" from industry. In particular, owing to earlier studies in connection with the needs of industry, convenient methods were found for the synthesis of a new group of derivatives of *N*-methylxanthines substituted in the 8-position (see Section III, subsection 1).

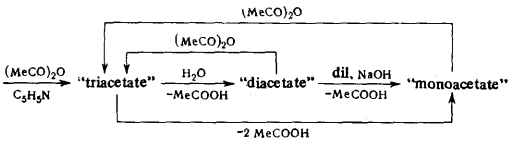
Moreover, these studies threw light on certain controversial problems concerning the structure of the compounds formed in the conversion of uric acid into 8-methylxanthine and permitted the use of the result for preparative purposes, namely for the synthesis of 9-methylpurine derivatives which had been hitherto unknown or difficult to obtain (see Section III, subsection 2).

Since the initial publication of the methods of preparation of 8-methylxanthines from uric acid[13], it has been discovered that this complex process proceeds via two stages. The first, which terminates after only brief heating with acetic anhydride (4–5 h), requires the presence of tertiary amines and is accompanied by the evolution of CO_2. The reaction product is a mixture consisting of a substance readily soluble in boiling water and a comparatively small amount of compound (II) which is virtually insoluble in it. A crystalline compound $C_8H_{10}N_4O_4$, which was believed to be an intermediate in the above process for half a century, is precipitated from the cooled aqueous filtrate.

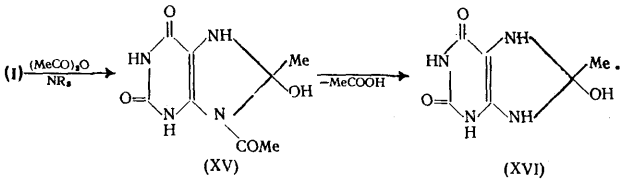
Indeed, it can be converted into compound (II) on prolonged heating with acetic anhydride. The second stage no longer requires the presence of tertiary amines and proceeds with elimination of acetic acid[34]. The first views concerning the course of the process were expressed at the same time[35] and a process mechanism was put forward, according to which the structure of 4,5-diacetamidouracil (XIV) was attributed to the intermediate and the compound $C_6H_8N_4O_3$ obtained from it by the hydrolytic elimination of one acetyl group in an alkaline medium was assumed to be the monoacetyl derivative of 4,5-diaminouracil (XIa or XIb).



In the first place we must note that fifty years later Bredereck et al.[36] established that the intermediate in the conversion of uric acid into 8-methylxanthine is not the compound $C_8H_{10}N_4O_4$, as believed previously, but a compound containing a further acetyl group ($C_{10}H_{12}N_4O_5$). It was found that it hydrolyses with elimination of one mole of acetic acid after only brief heating with water. They isolated this substance directly from the mixture which was untreated with water and was formed in the interrupted synthesis of compound (II) and also by treating with acetic anhydride the "intermediate compound" crystallised from water or the compound $C_6H_8N_4O_3$ obtained from the latter by alkaline hydrolysis†.



In 1923 Biltz and Schmidt published their first detailed study of the structures of "diacetate" and "monoacetate".[37] They suggested that both "diacetate" and "monoacetate" are bicyclic carbinols, namely, 9-acetyl-8-hydroxy-8-methyl-8,9-dihydroxanthine (XV) and 8-hydroxy-8-methyl-8,9-dihydroxanthine (XVI):



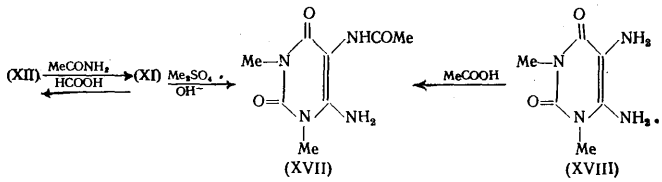
In 1953–1954, i.e. 30 years later, the structures of "triacetate", "diacetate", and "monoacetate" were revised in studies published almost simultaneously in the German Federal Republic[36,38,39] and in the Soviet Union[40–43].

It is remarkable that although their results were closely interrelated and many of their fundamental aspects were identical, their authors arrived at opposite conclusions concerning the "closed" (i.e. bicyclic) or "open" (i.e. uracil) structures of "diacetate" and "triacetate". "Monoacetate" was shown unanimously and by different methods to have the uracil structure (XI) and not the bicyclic carbinol structure (XVI).

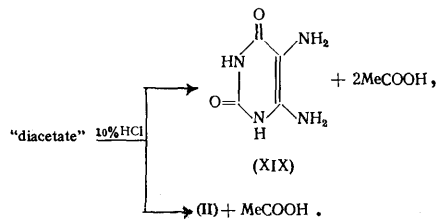
Structure (XI) of "monoacetate" was confirmed by many reactions, including the quantitative isolation of one mole of acetic acid at low pH, its formation from 4-amino-5-formamidouracil (XII) known previously[44] on treatment with acetamide, and finally its conversion into compound (XII) by heating with an excess of formic acid[33,36]. In addition, two specimens of "1,3-dimethylmonoacetate" (XVII) were

† For brevity, they suggested that the following names be given to the three compounds (these have been adopted in subsequent descriptions): "triacetate"—the true intermediate, "diacetate"—obtained by the crystallisation of "triacetate" from water, and "monoacetate"—obtained from "triacetate" or "diacetate" by the hydrolytic removal of two or one acetyl groups.

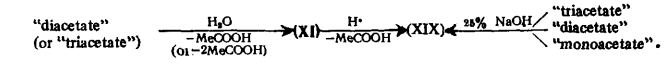
identified; one of them was obtained by heating 4,5-diamino-1,3-dimethyluracil (XVIII) with acetic acid and the other by methylating "monoacetate" (XI)[41]:



Both series of studies described demonstrated the error of Biltz and Schmidt's assertion[37] that "diacetate" is incapable of splitting off both acetyl groups on hydrolysis. The exact determination of the amounts of acetic acid distilled off during the hydrolysis of "diacetate" at low pH showed that it indeed never reaches two moles and is approximately one and a half moles. This was convincingly explained by the fact that, when "diacetate" is heated with inorganic acid, it can cyclise with formation of 8-methylxanthine[45]. The measured amounts of distilled acetic acid showed that in the acid hydrolysis of "diacetate", two parallel processes take place: (a) the hydrolysis of both acetyl groups and (b) the hydrolysis of one acetyl group accompanied by the formation of 8-methylxanthine via the second group. 8-Methylxanthine could be always isolated from the "diacetate" hydrolysis mixture[41]:

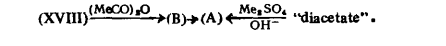


The quantitative isolation of two moles of acetic acid as a result of the hydrolysis of "diacetate" (and correspondingly three moles from "triacetate") can be achieved by their prolonged refluxing with water, which results in the formation of "monoacetate"[43], and subsequent hydrolysis of the latter in the presence of inorganic acids. On the other hand, 4,5-diaminouracil (XIX) was obtained in a yield exceeding 90% by treating "monoacetate", "diacetate", and "triacetate" with 25% sodium hydroxide solution[45]:



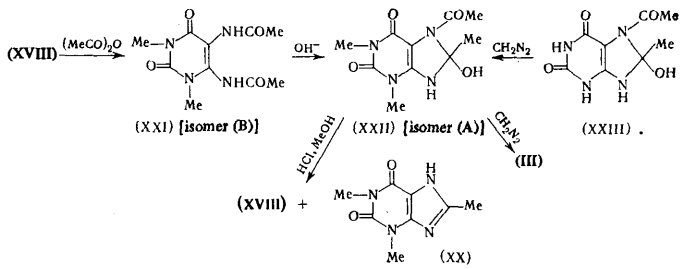
The preparation of the following methylated derivatives of "diacetate" was described in both studies: "tetramethyldiacetate" and two isomeric "dimethyldiacetates" (A) and (B), one of which was obtained by methylating "diacetate" with dimethyl sulphate in an alkaline medium [compound (A)]; its properties differed from those of the second dimethyl derivative obtained by heating 4,5-diamino-1,3-dimethyluracil (XVIII) with acetic anhydride [compound (B)].

It was shown that this is not a consequence of the different positions of the *N*-methyl groups, because compound (B) is readily converted into compound (A) by dissolution in dilute alkali and subsequent precipitation with acid or by refluxing in butyl alcohol[38,40]:

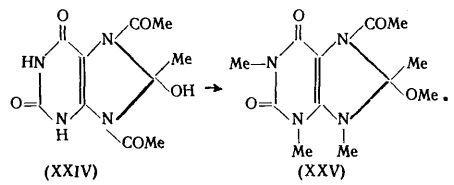


Compound (B) does not react with diazomethane and is readily hydrolysed by HCl in methanol with evolution of two molecules of acetic acid and by 20% acetic acid with evolution of one molecule of CH_3COOH.

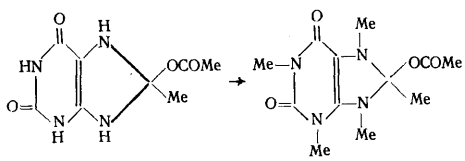
In contrast to (B), its isomer (A) readily reacts with diazomethane and is converted thereby into 1,3,7,8-tetramethylxanthine (III), but does not react at all with 20% acetic acid. The reaction with HCl in methanol results in the elimination of only 1.5 moles of acetic acid and the formation of a mixture consisting of a diamino-derivative (XVIII) and 1,3,8-trimethylxanthine (XX), i.e. behaves in the same way as the initial non-methylated "diacetate". The chemical behaviour of the isomer (B) led the German workers (Bredereck and coworkers) to the hypothesis that it is 4,5-diacetamido-1,3-dimethyluracil (XXI), which cyclises under the influence of alkali with formation of the dihydropurine isomer (A) (XXII). The fact that the latter can be obtained from "diacetate" by methylation of diazomethane suggested that the initial non-methylated "diacetate", obtained in the conversion of compound (I) into compound (II), has a bicyclic carbinol structure like "triacetate":



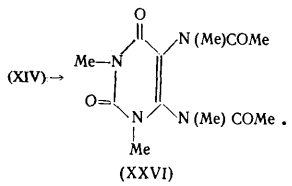
The German workers disagreed with Biltz and Schmidt[37] only as regards the position of the "hydrolysable" acetyl groups—at $N_{(7)}$ and not at $N_{(9)}$—and attributed structures (XXIII) and (XXIV) to "diacetate" and "triacetate" and structure (XXV) to "tetramethyldiacetate" obtained from them[38]:



They did not notice that not even traces of a methoxy-group could be detected in "tetramethyldiacetate" by analytical methods, although this finding ruled out the validity of their hypothesis concerning the structure of (XXV). The possibility of another bicyclic structure of "tetramethyldiacetate", which they did not consider, where the "hydrolysable" acetyl group is joined to the dihydroimidazole ring by an ester and not an amide linkage and all four methyl groups are joined to the ring nitrogen atoms, was disproved by an infrared spectroscopic study of "diacetate" and all its methylated derivatives[40].

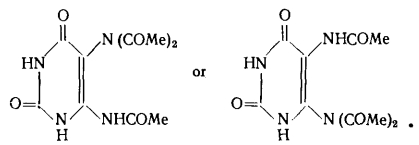


The absence of the methoxy-group from "tetramethyldiacetate" and the spectroscopic data thus disproved the possibility of any bicyclic structure of "tetramethyldiacetate" and suggested that it is 1,3-dimethyl-4,5-di(methylacetamido)uracil (XXVI), which in turn constituted important evidence in support of the validity of the structure (XIV) proposed initially for "diacetate"[40]:



(XXVI)

This structure of "diacetate" was confirmed by its capacity, mentioned above, to be hydrolysed comparatively readily with evolution of two moles of acetic acid when conditions ruling out the possibility of cyclisation are observed. The elimination of one acetyl group and the formation of "monoacetate", i.e. 5-acetamido-4-aminouracil (XXI) take place under such mild conditions (heating with water) that the opening of the imidazole ring in this reaction is unlikely[43]:

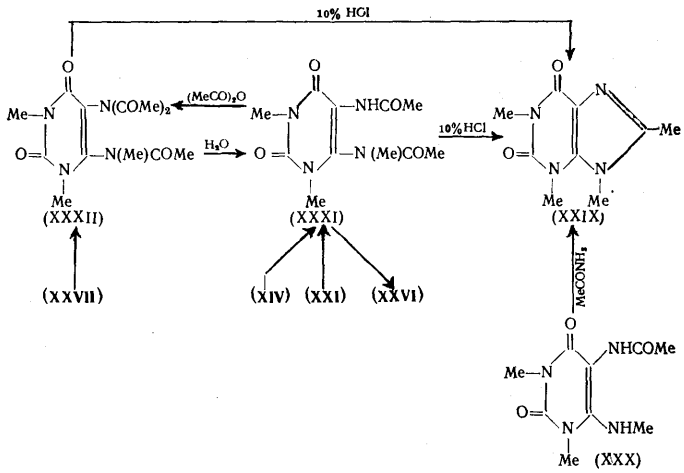


(XXVII) (XXVIII)

The choice between the two possible structures of "triacetate", (XXVII) and (XXVIII), was made by studying the reactions of "trimethyldiacetate", which was isolated for the first time from the reaction mixture obtained in the methylation of "diacetate". It was obtained also from "1,3-dimethyldiacetate" (XXI) and its methylation yielded "tetramethyldiacetate" (XXV).

It was found that the third methyl group of "trimethyldiacetate" is at the amino-group joined to $C_{(4)}$ (the position of the two other methyl groups at $N_{(1)}$ and $N_{(3)}$ gave rise to no doubts), since on heating with 10% hydrochloric acid a single molecule of acetic acid is split off and cyclisation with formation of 1,3,8,9-tetramethylxanthine (XXIX) takes place[42]. The latter was identified with methylisocaffeine, synthesised from 1,3-dimethyluramil[46] and also by condensing 5-acetamido-4-methylamino-1,3-dimethyluracil (XXX) with acetamide[38].

On the basis of the uracil structure of "tetramethyldiacetate" and the formation of methylisocaffeine as a result of the cyclisation of "trimethyldiacetate", the latter is 5-acetamido-4-acetylmethylamino-1,3-dimethyluracil (XXXI). When it is treated with acetic anhydride, it is acetylated to "trimethyltriacetate", the only possible structure of which is 5-diacetamido-4-acetylmethylamino-1,3-dimethyluracil (XXXII). It was identified with "trimethyltriacetate" obtained by methylating "triacetate" isolated directly from the reaction mixture obtained when uric acid interacts with acetic anhydride. This showed that the acetyl groups in "triacetate" are located in the same positions as in compound (XXXII), which fully confirmed that their structure is (XXVII)[47,48] and not (XXVIII)[42].



The cyclisation of (XXXI) and (XXXII) on treatment with inorganic acids led to the possibility of employing this reaction as a convenient method of synthesising methylisocaffeine (XXIX) which was previously difficult to obtain. The solutions formed as a result of the methylation of "diacetate" or "triacetate" are heated with an acid for this purpose. The highly soluble "trimethyldiacetate" (XXI) contained in these solutions is then converted into the comparatively sparingly soluble compound (XXIX), which crystallises in its entirety on cooling[49]. Its yield is 60–65% with respect to two stages (methylation and cyclisation) or 40–45% relative to uric acid (i.e. with respect to all three stages).

Methylisocaffeine (XXIX) obtained in this way subsequently serves as the starting material for the synthesis of hitherto unknown derivatives of 9-methylpurine.

III. SYNTHESES BASED ON *N*-METHYLATED 8-METHYLXANTHINES

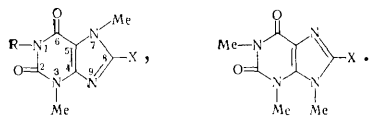
Both isomeric tetramethylxanthines synthesised from uric acid, i.e. 8-methylcaffeine (III) and 8-methylisocaffeine (XXIX), as well as 3,7,8-trimethylxanthine, i.e. 8-methyltheobromine (IV), were employed successfully to synthesise *N*-methylated purines: (1) xanthines (2,6-dioxopurines) substituted at $C_{(8)}$ and (2) 1,9-dimethylhypoxanthines (6-mono-oxopurines) and 9-methylpurines substituted at the carbon atoms of the pyrimidine ring‡.

1. Methylated Xanthines Substituted at $C_{(8)}$

In accordance with the difference between the positions of the *N*-methyl group of the imidazole ring (7- or 9-) in the initial compounds (III) or (IV) and (XXIX), these are

‡ In accordance with the aim of this review, it does not include questions concerning the synthesis of the isomeric derivatives of 3,7-dimethylhypoxanthine and 7-methylpurine, since the starting material for their synthesis is theobromine, which is not as a rule obtained from uric acid.

the parent compounds of two isomeric α- and β-series of $C_{(8)}$-substituted xanthines with different positions of the double bond in the ring, which sometimes differ significantly in their properties. The results of methylation in an aqueous alkaline medium[50,51], the rate of hydrolytic cleavage of the pyrimidine ring under the influence of alkaline agents[52], ultraviolet spectra[53,54], and certain other chemical and physical properties can serve as examples of such differences for α- and β-xanthines, in particular for compounds (III)–(VI), (XXIX), and (XXXIII):



(III, R = X = Me) (V, R = Me, X = H) (XXIX, X = Me)
(IV, R = H, X = Me) (VI, R = X = H) (XXXIII, X = H)

The first widely occurring stage in the reactions of all three 8-methyl derivatives of *N*-methylated xanthines (III), (IV), and (XXIX) is the substitution of the hydrogen atoms in the $C_{(8)}$-methyl group by chlorine. Such substitution is as a rule achieved by treatment with chlorine or sulphur chloride[15,18,24-28,55-60] and does not require vigorous heating[18,25,27]. The substitution of one or two hydrogen atoms in this methyl group by chlorine leads to the formation of mono- and di-chlorides[15,58-60,66] and the replacement of chlorine in such groups by other substituents leads to the synthesis of a wide variety of $C_{(8)}$ derivatives of caffeine (V)[56], theobromine (VI)[58,60-62], and isocaffeine (XXXIII)[59,63]. Compounds of this type may be obtained from 8-methylderivatives of *N*-methylxanthines also by another longer but more universal procedure based on the preliminary elimination of the $C_{(8)}$-methyl group by complete substitution with chlorine and subsequent hydrolysis[15,16,18,24-28,55-58].

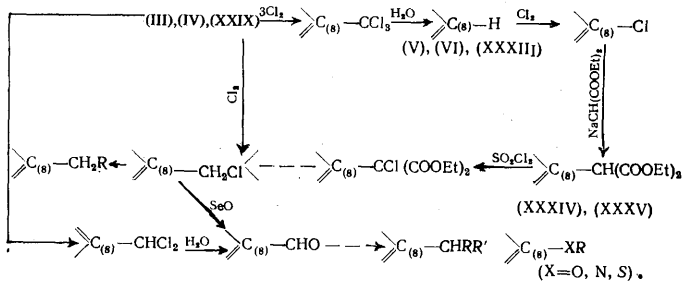
The substitution of a hydrogen atom in the 8-position by halogen[55,64-68] in compounds (V), (VI), and (XXIII) formed§ and condensation of 8-halogeno-*N*-methylxanthines with sodiomalonic and sodioalkylmalonic esters also makes it possible to prepare various $C_{(8)}$-derivatives. Caffeine-8-malonic ester (XXXIV) and isocaffeine-8-malonic ester (XXXV) exhibit a fairly high acidity[65,69], exceeding that of other monosubstituted malonic esters and of malonic ester itself and are produced in the condensation reaction as crystalline sodium derivatives, which are formed from the unreacted part of the sodiomalonic ester. Therefore the normal termination of the reactions always requires the use of two moles of sodiomalonic ester per mole of the chloride:

$$\rangle C_{(8)}-Cl + 2NaCH(COOEt)_2 \xrightarrow{-NaCl} \rangle C_{(8)}-CH(COOEt)_2 + NaCH(COOEt)_2 \rightarrow \rangle C_{(8)}-C(Na)(COOEt)_2 + CH_2(COOEt)_2.$$

The electron-accepting properties of the purine molecule lead to an enhancement of the polarity of the C–H bond of the malonic acid group in compounds (XXIV) and (XXXV).

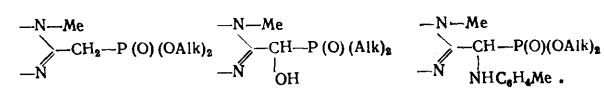
This influence is general and is observed for other *C*-malonic acid derivatives of various purine systems, regardless of the position of the malonic acid residue in the purine molecule—at $C_{(8)}$,[70-73] at $C_{(6)}$,[74,75] or at $C_{(2)}$.[76-78] This influence is shown also by the fact that the halogen atom in the malonic acid residue in purinylhalogenomalonic esters reacts as a halogen cation[79] and also by the capacity of purinylmalonic, alkylmalonic, and acylaminomalonic esters to split off, on heating with alkoxides in an alcoholic medium, one of the two ethoxycarbonyl groups with formation of esters of the corresponding purinylmonocarboxylic acids and of the carbonic ester[80-82].

Subsequent reactions of the malonic acid residue in the diesters (XXXIV) and (XXXV) as well as the conversion of 8-monochloro- and dichloro-methyl derivatives obtained by direct chlorination of compounds (III), (IV), and (XXIX), permitted a fairly wide variation of the nature of the substituent linked to $C_{(8)}$ in *N*-methylated xanthines and the synthesis via the two schemes discussed above of compounds with a wide variety of substituents R—derivatives of alkanoic acids with straight or branched chains[63,65,69,71-73,83-90], aldehydes, alcohols[59,60,61,72,85,87-90], amines[52,63,85,88-92], derivatives of α-alanine substituted with a xanthine molecule at the β-carbon atom[58,59,88,92] (cf. Refs. 74–78), and certain others (see, for example, Refs. 93–95):



Lugovkin synthesised a group of purinylphosphonic acid esters from 8-monochloro and dichloromethyl-*N*-methylxanthines (1,3,7-, 1,3,9-, and 3,7-derivatives) via the Arbuzov reaction. Diesters of the corresponding purinylmethylphosphonic acids (XXXVI) were obtained by the condensation of 8-monochloromethylcaffeine[96] (and later also 2-chloro-6-monochloromethyl-9-methylpurine[74,97]) with trialkyl phosphites and diesters of α-hydroxy-8-purinylmethylphosphonic acids (XXXVII) were obtained by the reaction of dialkylphosphorous acids with caffeine-8-aldehyde and theobromine-8-aldehyde[98,99].

A series of dimethyl esters of 8-purinyl-(*p*- and *m*-tolylamino)methylphosphonic acids (XXXVIII) were synthesised by treating with dialkylphosphorous acids 8-xanthinylazomethines obtained by the condensation of the above aldehydes with *m*- or *p*-toluidine[100]:

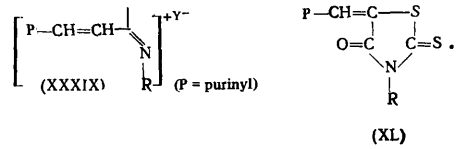


(XXXVI) (XXXVII) (XXXVIII)

Lugovkin investigated the condensation of *N*-methylated xanthine-8-aldehydes with the active methylene groups of the alkiodides of α- and β-picolines, quinaldine, lepidine, and 2-methylbenzothiazole and its derivatives[101-103] and also with 3-alkyl- and 3-phenylrhodanines[104], which yielded the quarternary salts of various heterocyclic systems with *N*-methylated xanthine-8-ylidene substituents

§ It is self-evident that the synthesis of uric acid is not obligatory for the synthesis of caffeine which is nowadays manufactured by another synthetic procedure or isolated from natural materials. However, this scheme may be regarded as entirely reliable for the preparation of derivatives of 9-methylpurines, and it has many advantages over other versions of their synthesis.

(XXXIX) and also purine rhodanines with the general formula (XL):



(XXXIX) (P = purinyl)

(XL)

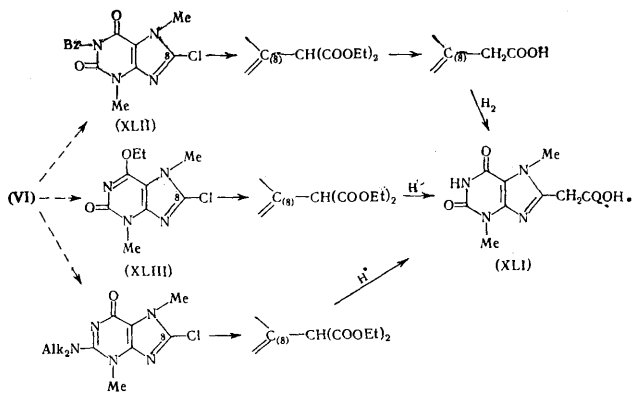
The interaction of *N*-methylated 8-chloroxanthines with amines, alkoxides, and other nucleophilic agents leads readily to the formation of the corresponding xanthines with C–N, C–O, and C–S bonds at the $C_{(8)}$ carbon atom.

Such reactions and also the direct substitution of the hydrogen atoms of the $C_{(8)}$-methyl group by chlorine discussed above and the subsequent conversion of the mono-, di-, and tri-chlorides takes place in more or less the same manner for *NNN*-trimethylxanthines and those *N*-methylated xanthines where one or two ring hydrogen atoms are unsubstituted (see, for example, Golovchinskaya et al.[52]).

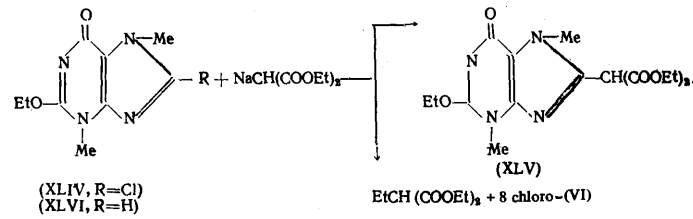
In contrast to these reactions, the condensation of 8-chloro-derivatives of *NN*-dimethylxanthines and *N*-monomethylxanthines with sodiomalonic ester is much more complicated than the analogous condensation of *NNN*-trimethylxanthines, i.e. of 8-chlorocaffeine and 8-chloroisocaffeine, since it requires a preliminary introduction of protecting groups. *N*-Benzylation or the introduction of *C*-alkoxy groups are usually employed for this purpose. Catalytic reduction is used to remove the benzyl group[62,72,89,105,106] and the alkoxy-group is eliminated hydrolytically[71–73,88].

Both methods of protection can be clearly illustrated by the synthesis of theobromine-8-acetic acid (XLI) and its derivatives from 1-benzyl-8-chlorotheobromine (XLII) and from 8-chloro-6-ethoxy-3,7-dimethylhypoxanthine (XLIII)[72,107].

Recently yet another method of synthesising theobromine-8-acetic acid from theobromine (VI) has been discovered; it is based on the fact that the alkylamino-groups linked to the $C_{(2)}$ atom of 3,7-dimethylhypoxanthine are readily split off on heating with inorganic acids[108]. Therefore such groups can be successfully employed at $C_{(2)}$ instead of alkoxy-groups at $C_{(6)}$ for protection in the condensation of 8-chlorotheobromine with sodiomalonic ester. They are eliminated with regeneration of the xanthine structure and simultaneous hydrolytic cleavage of the malonic acid residue[109]:



An interesting fact was observed in an attempt to synthesise the acid (XLI) from 8-chloro-2-ethoxytheobromine or 8-chloro-2-ethoxy-3,7-dimethylhypoxanthine[110–111] (XLIV), i.e. from an isomer of compound (XLIII). The yield of the condensation product, 2-ethoxytheobromine-8-malonic ester (XLV), was found to be appreciably lower than the yield of the condensation product obtained from the 6-ethoxy-derivative (50% instead of 80%), because the condensation of (XLIV) was accompanied by a parallel reaction involving the ethylation of the malonic ester owing to the cleavage of the ethoxy-group at $C_{(2)}$. In this case, the final reaction products were, apart from (XLV), ethylmalonic ester (yield 42%) and 8-chlorotheobromine:



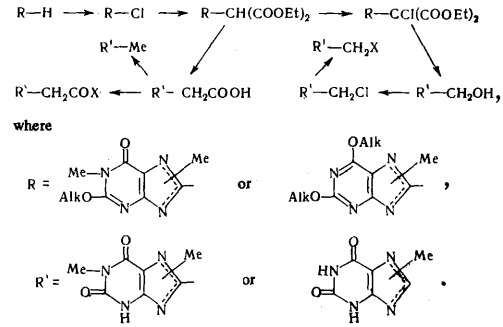
(XLIV, R=Cl) (XLVI, R=H)

(XLV)

$EtCH(COOEt)_2$ + 8 chloro-(VI)

The yield of ethylmalonic ester increases and reaches 92% when the possibility of the competing condensation reaction is excluded, i.e. when 2-ethoxy-theobromine (XLVI), which does not contain a chlorine atom at $C_{(8)}$, is allowed to react with sodiomalonic ester. The capacity of compounds (XLIV) and (XLVI) to behave as ethylating agents has been confirmed also in other reactions[112].

The isomeric 2-ethoxy-1,9-dimethylhypoxanthine (XLVII) and 2-ethoxy-1,7-dimethylhypoxanthine (XLVIII) and their 8-chloroderivatives (XLIX) and (L)[113–116] also alkylate malonic ester, but the main reaction products formed are the corresponding 2-ethoxypurinyl-8-malonic esters[112]. As a result, both 2-alkoxydimethylhypoxanthines [(XLVII and XLVIII) and also 2,6-dialkoxy-7-methylpurine (LI) and 2,6-dialkoxy-9-methylpurine (LII); see below] were used as the starting materials for the synthesis in satisfactory yields of a series of derivatives of 1,7- and 1,9-dimethylxanthines and also 7- and 9-monomethylxanthines substituted by various groups in the 8-position[72,113]:



It was suggested that the reason why 2-ethoxytheobromine (XLVI) and its 8-chloro-derivative (XLIV) are more active ethylating agents than compounds (XLVII)–(L) is associated with the *p*-quinonoid structure of the pyrimidine part of the molecule, which entails an additional decrease of electron density at $C_{(2)}$ and a consequent loosening of the bond between the oxygen in the ethoxy-group and the carbon atom of the alkyl group.

The real reason for the inability of 8-chloro-6-ethoxy-theobromine (XLIII), mentioned above, to alkylate malonic ester is probably the steric effect of the $N_{(7)}$-methyl group, which is in the *peri*-position relative to the $C_{(8)}$ reaction centre[112].

LCAO-MO calculations using the parameters of Pullman's system for the compounds (XLVI), (XLIV), (XLVII)–(L), 1,7-, 1,9-, and 3,7-dimethylhypoxanthines, 3,7-dimethyl-2-oxo-2,3-dihydropurine[67–69] and the study of their ^{1}H NMR spectra yielded a satisfactory qualitative correlation between the experimental and calculated data characterising the reactivity of the substituents (the ethoxy-group at C$_{(2)}$ and the chlorine atom at C$_{(8)}$) in the reactions discussed above[117].

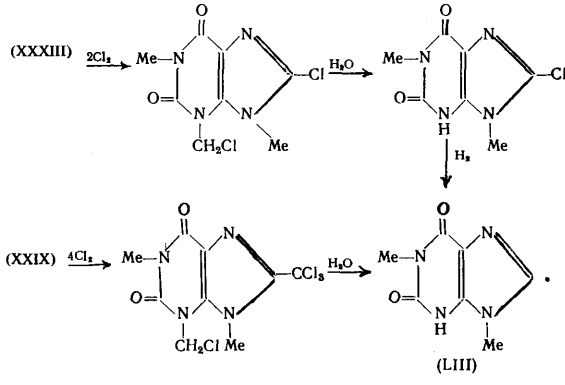
In conclusion of this section, it should be noted that the difference between α- and β-xanthines is shown to only a slight degree in the reactions enumerated above.

2. 9-Methylpurine Derivatives Substituted in the Pyrimidine Ring

a. Preparation of 1,9-dimethylxanthine from 8-methylisocaffeine. Substitution of tetramethylxanthines with chlorine in the C$_{(8)}$-methyl group and directly at C$_{(8)}$ in *NNN*-tri- and *NN*-di-methylxanthines takes place in the α- and β-series without significant differences, while in the substitution with chlorine in the *N*-methyl groups (reactions requiring higher temperatures[18,25,118–121] and the use of an excess of the chlorinating agent) certain differences are observed.

The replacement by chlorine of some of the hydrogen atoms in the *N*-methyl group of 8-chlorocaffeine[118–120] and 8-trichloromethylcaffeine[18,24,25] with subsequent hydrolytic elimination of the *N*-monochloromethyl group constitutes the basis of the methods of industrial synthesis of theophylline (VII) from caffeine[122] or uric acid, which have been known for a long time.

The chlorination of isocaffeine (XXXIII) and its 8-methyl derivative (XXIX) and subsequent hydrolysis yielded 8-chlorodimethylxanthine and dimethylxanthine containing *N*-methyl groups in the 9-position; on the other hand, the chloromethyl groups at N$_{(3)}$ in the pyrimidine ring were eliminated[53,123–129]:



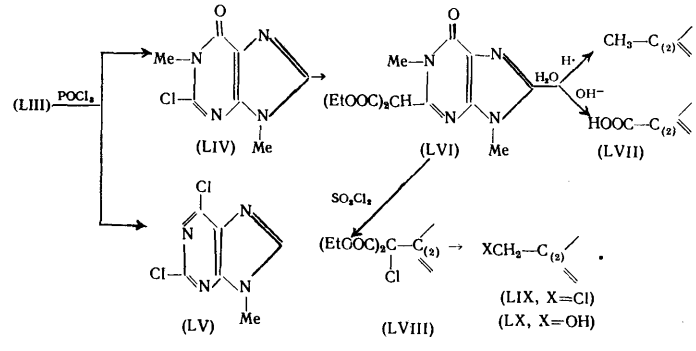
The observed difference in the order of substitution by chlorine of the hydrogen atoms in the *N*-methyl groups of *NNN*-trimethylxanthines of the α- and β-series led to a comparatively simple and short method for the conversion of compound (XXIX) into 1,9-dimethylxanthine (LIII)[130], which had been synthesised hitherto by more time-consuming procedures[127,128,131]. Owing to the ease of the new method of synthesising (LIII), it has become the starting material for the synthesis of many derivatives of 1,9-dimethylhypoxanthine substituted at C$_{(2)}$ and also of 9-methylpurine substituted at C$_{(2)}$ and at C$_{(6)}$.

b. Synthesis of derivatives of 1,9-dimethylhypoxanthine substituted at C$_{(2)}$. When 1,9-dimethylxanthine is heated with phosphoryl chloride, 2-chloro-1,9-dimethylhypoxanthine (LIV) is formed in 55% yield with an admixture of about 10% of 2,6-dichloro-9-methylpurine (LV).[128] When the monochloro-derivative (LIV) is heated with aqueous solutions of ammonia and primary and secondary amines and also with alcoholic solutions of thiourea and sodium alkoxides at temperatures below 100°C, derivatives of 1,9-dimethylhypoxanthine substituted at C$_{(2)}$ by various groups via the N, S, and O heteroatoms are formed comparatively readily[113]. 2-Amino-1,9-dimethylhypoxanthine had been obtained previously by the methylation of methylguanine[51].

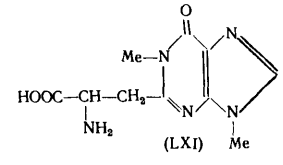
The high reactivity of chlorine in 2-chloro-1,9-dimethylhypoxanthine (LIV) was employed for malonic ester synthesis[76].

Like *NNN*-trimethylxanthine-8-malonic ester and *NN*-dimethyl- and *N*-monoethyl-hypoxanthine-8-malonic esters mentioned above, the diester (LVI), obtained in this process has a relatively high acidity constant and therefore two moles of sodiomalonic ester are employed per mole of (LIV) to obtain a high yield of the diester. Hydrolysis of compound (LVI) in an alkaline medium yielded 1,9-dimethylhypoxanthine-2-acetic acid (LVII), its esters, and amides. In contrast to xanthine-8-acetic acids, this acid readily splits off CO_2 at a low pH and therefore hydrolysis of the diester in the presence of inorganic acids leads to the formation of 1,2,9-trimethylhypoxanthine.

When the diester (LVI) is treated with sulphuryl chloride, 1,9-dimethylhypoxanthine-2-chloromalonic ester (LVIII) is obtained; depending on the conditions, the latter can be hydrolysed to the chloromethyl derivative (LIX) or the hydroxymethyl derivative (LX):



A group of derivatives of 1,9-dimethylhypoxanthine substituted at C$_{(2)}$ via a C–C bond, including β-(1,9-dimethylhypoxanthin-2-yl)-α-alanine (LXI), an analogue of β-(8-purinyl)-α-alanine mentioned above, was obtained by treating the chloro-derivative (LIX) with various nucleophilic agents[76]:

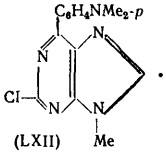


c. Synthesis of 9-methylpurine derivatives substituted at C$_{(2)}$ and at C$_{(6)}$. 9-Methylpurine derivatives substituted at C$_{(2)}$(R) and at C$_{(6)}$(R′) were obtained from 1,9-methylxanthine via two procedures:

with intermediate formation of 2,6-dichloro-9-methylpurine (LV) or from compound (LIV) by substituting the chlorine at $C_{(2)}$ with subsequent conversion of 2-R-1,9-dimethylhypoxanthine into 2-R-6-chloro-9-methylpurine and the subsequent replacement of chlorine by the required substituent R'.[114]

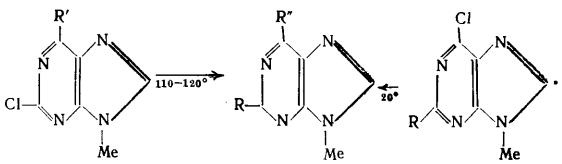
The formation of 2,6-dichloro-9-methylpurine (LV)[128] as the main product from compound (LIII) is a complicated process requiring heating with phosphoryl chloride at a high temperature (about 160°C)[132] or the addition of agents such as tertiary amines or phosphorus pentachloride.

Dimethylxanthine (LIII) can be converted into dichloropurine (LV) by heating with phosphoryl chloride in the presence of dimethylaniline, by analogy with the synthesis of 2,6-dichloro-7-methylpurine from theobromine[133], but the yield of the dichloro-derivative does not exceed 30–32%. The product is a bright-yellow substance (LXII), which was identified by ^{1}H NMR spectroscopy with a substance which had been obtained by the interaction of 2-chloro-1,9-dimethylhypoxanthine (LIV) with $POCl_3$ and dimethylaniline[134–136]:



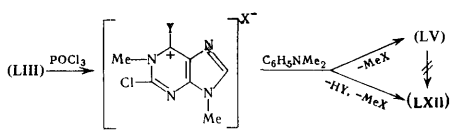
(LXII)

The structure of compound (LXII) is confirmed by its similarity to 2-chloro-6-R'-9-methylpurines in which R' is a dimethylamino- or a benzylamino-group (the substitution of chlorine by amines requires prolonged heating at 110–120°C). The reactivity of compound (LXII) is very much lower than that of the highly reactive 2-R-6-chloro-9-methylpurines, which undergo nucleophilic exchange reactions even at room temperature[137]:



Condensation with dimethylaniline was found to be a side reaction taking place simultaneously and not a secondary process involving the final dichloro-derivative (LV) after its formation. Its comparatively high reactivity of the chlorine atom at $C_{(6)}$ in this dichloro-derivative was still found to be inadequate to ensure para-condensation with dimethylaniline, as shown by experiments in which compound (LV) was heated with dimethylaniline in phosphoryl chloride.

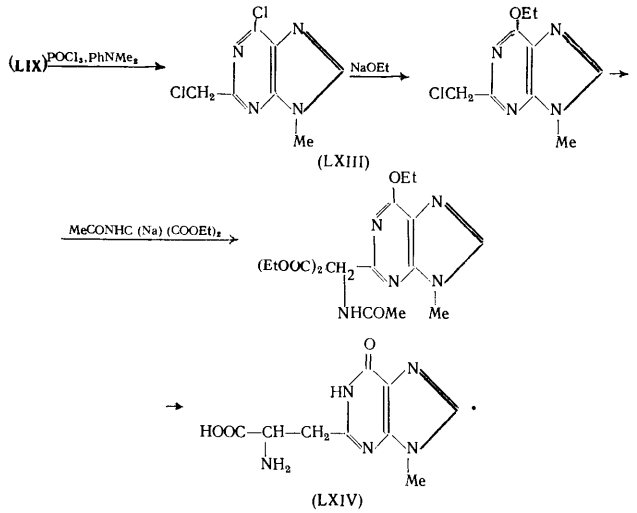
Evidently a purine compound in which the $C_{(6)}$ atom is more electrophilic takes part in the para-condensation reaction. It was suggested that an intermediate of the amidochloride type[138–140], which is partly cleaved with formation of a dichloro-derivative and partly condenses with dimethylaniline and only then splits off the $N_{(1)}$-methyl group, should be regarded as responsible for the formation of the para-condensation product. The primary product of such para-condensation is a precursor of compound (LXII), which was isolated[138]:



(X, Y = Cl, Cl or Cl, $OPOCl_2$)

The validity of this interpretation of the process is partly confirmed by the analogy with the isomeric dimethylxanthine of the α-series, namely theobromine: its reaction with dimethylaniline and phosphoryl chloride led to the isolation, apart from 2,6-dichloro-7-methylpurine, of the primary para-condensation products retaining the $N_{(3)}$-methyl group in the pyrimidine ring[141].

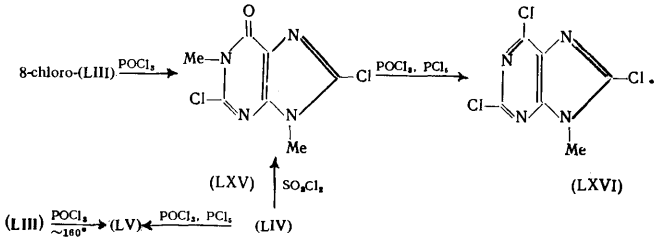
Certain derivatives of 1,9-dimethylhypoxanthine containing substituents at $C_{(2)}$ and linked to the purine molecule via a heteroatom split off the $N_{(1)}$-methyl group comparatively readily and are converted into the corresponding 2-R-6-chloro-9-methylpurines as a result of heating with phosphoryl chloride without the addition of tertiary amines or phosphorus pentachloride[142]. However, when there is a carbon–carbon bond at $C_{(2)}$, the reaction requires the presence of dimethylaniline and takes place with charring. For example, 2-chloromethyl-1,9-dimethylhypoxanthine (LIX) gives not more than 40% of 6-chloro-2-chloromethyl-9-methylpurine (LXIII)—a compound from which yet another purinylalanine (LXIV) was synthesised according to the following scheme[143]:



The replacement of dimethylaniline by other tertiary amines (cf., for example, Robins and Christensen[144]) in order to eliminate the parallel para-condensation process mentioned above leads to a considerable increase of the yield of the dichloro-derivative (LV). Thus, when dimethylxanthine (LIII) was heated with phosphoryl chloride and triethylamine hydrochloride, compound (LV) was obtained in 70–75% yield[109]. This compound can be obtained also in satisfactory yield (60–65%) when phosphorus pentachloride is employed instead of tertiary amines.

If phosphorus pentachloride is present in the reaction mixture from the very beginning of the heat treatment of compound (LIII) in the presence of phosphoryl chloride, a parallel process involving electrophilic substitution by chlorine at $C_{(8)}$ takes place, the 8-chloro-derivative of compound (LIII) undergoing subsequently the same reactions as the initial compound (LIII). Therefore ultimately, when phosphoryl chloride and phosphorus pentachloride act simultaneously on compound (LIII), one obtains from the reaction mixture, after treatment with water, a mixture which is difficult to resolve and which consists of the monochloro-derivative (LIV), the dichloro-derivative (LV), 2,8-dichloro-1,9-dimethylhypoxanthine (LXV), and 2,6,8-trichloro-9-methylpurine (LXIV)[145,146].

The chloro-derivatives (LXV) and (LXVI) proved to be identical with the specimens of the same compounds synthesised in other ways:



On the other hand, derivatives of 9-methylpurine containing a chloro-substituent in the pyrimidine ring, namely the chloro-derivatives (LIV) and (LV), are incapable of being substituted by chlorine at $C_{(8)}$ on treatment with PCl_5, in contrast to the initial xanthine (LIII), and therefore cannot serve as the starting materials for the synthesis of compounds (LXV) and (LXVI) in this reaction.

These observations agree with the general rules of electrophilic halogenation of the purine system in the 8-position according to which this is possible only when the molecule contains electron-donating groups capable of compensating the electron-accepting influence of the pyrimidine ring relative to the imidazole ring[147]. According to this rule, the presence of a chlorine atom in the pyrimidine ring decreases the nucleophilicity of the $C_{(8)}$ ring carbon atom and prevents halogenation at this position. The chloro-derivative (LIV) can be converted into the 8-chloro-derivative (LXV) only as a result of a prolonged reaction with SO_2Cl_2 (in a yield not exceeding 25%) but not by treatment with PCl_5. The dichloro-derivative (LV) does not react even with SO_2Cl_2.

A method for the synthesis of the dichloro-derivative (LV) from dimethylxanthine (LIII) is based on such relations; it consists in heating compound (LIII) with $POCl_3$ until the disappearance of the initial xanthine from the reaction sphere and the subsequent interaction of the reaction mixture with PCl_5.[133]

The replacement of the chlorine atoms in the dichloro-derivative in compound (LV) by identical or different atoms or groups makes it possible to obtain derivatives of 9-methylpurine with various combinations of substituents at the carbon atoms of the pyrimidine ring.

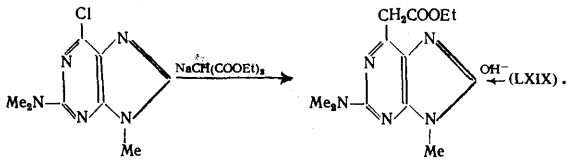
Owing to the much higher reactivity of the chlorine linked to $C_{(6)}$ in the initial chloro-derivative compared with the chlorine at $C_{(2)}$, it is possible to obtain from this compound 6-R′-2-chloro-9-methylpurines (R′ = OAlk, NHR″, SH, etc.) under very mild conditions after which the chlorine at $C_{(2)}$ can be reduced or replaced by other groups under more severe conditions[137,148]. It is self-evident that, when R = R′, both chlorine atoms are substituted simultaneously.

The non-equivalence of the chlorine atoms in the initial compound (LV) makes it possible to obtain from it derivatives of 9-methylpurine substituted at $C_{(6)}$[149,150] via the scheme adopted for the condensation of halogenopurines with sodiomalonic ester (see above). In 2-chloro-9-methylpurine-6-malonic ester (LXVII), the chlorine atom at $C_{(2)}$ may be reduced or replaced by another substituent [for example $N(CH_3)_2$] with formation of the corresponding diesters (LXVIII) and (LXIX). When the diesters (LXVII)–(LXIX) are heated with a dilute inorganic acid, 6,9-dimethylpurine (LXX), 2-R- (LXX), (LXXI, R = Cl), and [(LXXXII, R = $N(CH_3)_2$] are obtained.

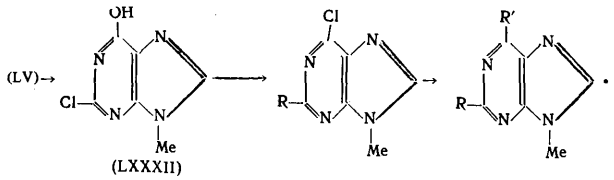
On treatment with SO_2Cl_2, the diesters (LXVII)–(LXIX) are converted into the corresponding purine-6-chloromalonic esters (LXXIII)–(LXXV), which are converted by hydrolysis at a low pH into 6-chloromethylpurines (LXXVI)–(LXXVIII). The yield of the conversion of (LXXIV) into (LXXVII) does not exceed 18%, since the main reaction product is found to be 6-hydroxy-9-methylpurine (LXXIX)[149], which is formed as a result of the cleavage of the C–C bond between $C_{(6)}$ of the 9-methylpurine molecule and the carbon atom of the chloromalonic group. Such hydrolytic cleavage of this bond is evidently a result of the high electrophilicity of the $C_{(6)}$ ring carbon atom. It is apparently also responsible for the capacity of the chlorine in the chloromethyl and chloromalonic groups of compounds (LXXIII)–(LXXVIII) to react vigorously as halogen cations and in particular to be reduced rapidly in KI solution with evolution of I_2 (see Scheme 3).

The chlorine in 6-chloromethylpurines (LXXVI)–(LXXVIII) can be substituted comparatively readily whereby the synthesis of a wide variety of $C_{(6)}$ derivatives of 9-methylpurine, including three β-(9-methyl-2-R-purin-6-yl)-α-anilines [(R = Cl, H, and $N(CH_3)_2$] can be achieved comparatively readily.

2-Chloro-9-methylpurine-6-carboxylic acid (LXXX) was obtained by the oxidation of the dichloro-derivative (LXXVI) in an alkaline medium and was converted into 2-dimethylamino-9-methylpurine-6-carboxylic acid (LXXXI). It is decarboxylated only on fairly strong heating, in contrast to the corresponding 2-R-9-methylpurine-6-acetic acids [R = Cl, H, and $N(CH_3)_2$], which split off CO_2 extremely readily. Quite stable esters of the latter were obtained from the diesters (LXVII)–(LXIX) by hydrolysis with NaOH in an aqueous-alcoholic medium[150] and one of them [R = $N(CH_3)_2$] is formed also by the condensation of 6-chloro-2-dimethylamino-9-methylpurine with sodiomalonic ester, since the reaction is accompanied by the splitting off of the ethoxycarbonyl group:

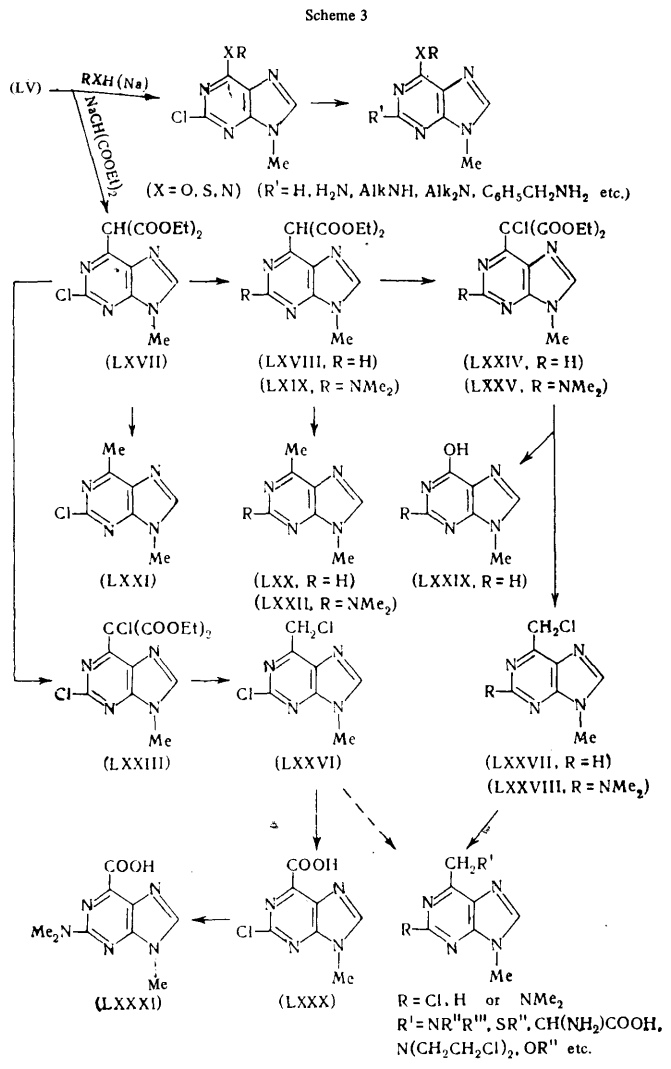


2,6-Disubstituted 9-methylpurines with various substituents at $C_{(2)}$ and $C_{(6)}$ can be synthesised from the dichloro-derivative (LV) also via another scheme with the intermediate formation of 2-chloro-6-hydroxy-9-methylpurine (LXXXII). The replacement of the chlorine in this compound at $C_{(2)}$ by various groups and subsequent introduction of chlorine at $C_{(6)}$ by treatment with $POCl_3$ and its subsequent substitution yield 2,6-disubstituted derivatives of 9-methylpurine containing all kinds of substituents at $C_{(6)}$, including the most reactive groups[113]:



The chloro-derivative (LXXXII) is formed in 82% yield after heating the dichloro-derivative (LV) for 5 h with 1 *N* acid. More prolonged heat treatment or the use of more

Scheme 3

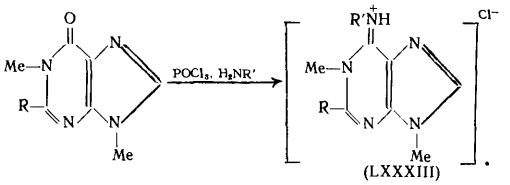


concentrated acid leads to the hydrolytic elimination of the second chlorine atom too, i.e. to the regeneration of the xanthine structure.

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The reactions of 1,9-dimethylxanthine described in this section do not exhaust the wide variety of processes in which the compound may be involved and all the possibilities of its employment for synthetic purposes. In particular, it does not include certain aspects of the reaction of 1,9-dimethylxanthine with phosphorus chloro-compounds, which require separate consideration and do not fit within the framework of the present review.

Brief mention should also be made of the synthesis of 6-imino(or alkylamino-)-1,9-dimethylpurines (LXXXIII)—analogues of 1-alkyl-6-iminopurines, which were obtained for the first time in the 1960's either by the alkylation of adenosine[151-154] or by synthesis from 3-amino-2-cyano-1-methyl-imidazole[155]. The hydrochlorides (LXXXIII) were formed as a result of treatment with aqueous solutions of ammonia or amines of compounds of the amidochloride type obtained by treating 1,9-dimethylxanthine (LIII) or 2-R-1,9-dimethylhypoxanthines (R = Cl, CH_3, NHAlk, etc.) with phosphoryl chloride[156]:



In contrast to the syntheses described previously, this scheme makes it possible to vary widely the substituents in the exocyclic imino-group of compound (LXXXIII) and at $C_{(2)}$ (cf. Nikolaeva et al.[157]).

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Ordzhonikidze All-Union Institute
of Chemistry and Pharmacology,
Moscow

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Polarographic Catalytic Currents of Complexes of Metals in Catalysis by a Ligand

Ya.I.Tur'yan

This review gives the characteristics of catalytic systems and results on the kinetics and mechanism of electrode chemical reactions, describes methods of determining the instability constants of complexes from the catalytic currents and the analytical use of catalytic boundary waves, and makes a comparison with results on corresponding non-electrode reactions of complex formation.
Among the bulk electrode chemical processes considered are theoretical and experimental results on an electrode reaction with two successive rate-determining chemical stages, and also on a double catalytic effect: that of the ligand and that of an addition of a polarographically active complex which is regenerated at the electrode.
The kinetics and mechanism of processes involving an adsorbed ligand-catalyst have been analysed on the basis of a concept of heterogeneous parallel reactions of complex formation.
There is a bibliography of 168 references.

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I. INTRODUCTION

The prewaves of the polarographic wave of the aquo-ions of a metal, linked with the participation of polarographically active complexes (PAC) in the electrode process during catalysis by a ligand, were termed[1,2] catalytic prewaves (points) of the metal complexes. Here we will not consider the catalytic currents of complexes in catalysis by the ions of a metal[3], the catalytic release of hydrogen, and the catalytic effect of the ligand in the presence of an inhibitor of the electron transfer stage[4], although this effect shows certain resemblances[5,6] to the catalytic influence of the ligand in the absence of an inhibitor.

The characteristics of catalytic currents of metal complexes in catalysis by a ligand are: (1) the prewaves arise at potentials that are more positive (cathodic)[7-12] or more negative (anodic)[11] than the reduction or oxidation potentials respectively of the aquo-ions of the metal; (2) a catalytically active ligand can be either charged[7] or electrically neutral[9]; (3) in the PAC the metal ions are reduced or oxidised with regeneration at the electrode of the ligand, which again participates in the formation of PAC[1,2]; however, when there is an excess of the ligand

(prewaves arise either when there is an excess of the ligand or when there is an excess of the metal ions)[13,14] or when the PAC is of low stability this phenomenon does not play a significant part; (4) the prewaves are of a kinetic nature[1,2,7-12], and increase with the concentration of the ligand, in many instances reaching the limit of the diffusion wave of the aquo-ions of the metal. However, when ligand adsorbed on the electrode participates in the formation of PAC, the prewave limiting current, having reached the region of diffusion current corresponding to potentials of maximal adsorption of the ligand, can fall again as the potential is changed, owing to partial desorption of the ligand (minimum on the polarisation curve)[8]; (5) the prewaves can exceed the initial diffusion wave of the aquo-ions of a metal when the solution contains, in addition to the ligand, certain components which regenerate PAC at the electrode. When components which do not form complexes are chosen the nature of the PAC remains unchanged[15,17].

Polarographically catalytic currents of metal complexes in catalysis by a ligand are of theoretical and practical importance: in electrocatalysis (especially chemical factors), electrodeposition (mechanism of the effect of a catalytically active ligand), the chemistry of coordination compounds (new methods of investigation of the instability constants of complexes and of the kinetics of complex formation, including the kinetics of complex formation under heterogeneous conditions), and analytical chemistry (polarographic determination of metals in the presence of catalytically active ligands and in a newer direction—determination of the ligands themselves with the aid of the prewaves). All these aspects of this problem will be covered in the present review.

II. CATALYTIC SYSTEMS

The choice of metal ions for the production of these catalytic prewaves is determined mainly by the presence of a high overpotential in the reduction or oxidation of the corresponding aquo-ions of the metal[18].

Catalytically active ligands can belong to various classes of inorganic and organic compounds, usually readily adsorbed on an electrode.

Usually prewaves have been observed in aqueous solutions, but there have been examples of catalytic currents in non-aqueous or mixed solvents[19-23].

A large number of catalytic systems are known (with the exception of the two examples of an anodic process given below, all cathodic processes): Ni^{II}–NCS^-,[7,10,12,24-29] Ni^{II}–Cl^- (Br^-, I^-),[19,20,23,30] Ni^{II}–pyridine and its alkyl, amino-, and hydroxo-derivatives,[1,2,9,14,21,29,31-42] Ni^{II}–1,2- and 1,5-diaminonaphthalenes,[2] Ni^{II}–3,4-diaminotoluene,[2] Ni^{II}–3,4-diaminobenzoic acid,[2] Ni^{II}–4,4′-diaminostilbene-2,2′-disulphonic acid,[2] Ni^{II}–aminoethylpiperazine,[2] Ni^{II}–2,2′-bipyridyl,[2] Ni^{II}–2-aminoethanol,[2] Ni^{II}–*o*-phenylenediamine,[2,43-51] Ni^{II}–*p*-phenylenediamine,[51] Ni^{II}–ethylenediamine,[52] Ni^{II}–thiourea and its derivatives[53-60], Ni^{II}–cysteine[61], Ni^{II}–selenocysteine[62], Ni^{II}–*o*,*o*′-diethyldithiophosphate[63], Ni^{II}–xanthogenate[22], Ni^{II}–thiosemicarbazide[57], Ni^{II}–rubeanic acid[57], Ni^{II}–unithiol[57], Co^{III}(ammonia complex)–Cl^-(Br^-),[64,65] Co^{II}–ethylenediamine (anodic process),[66] Co^{II}–cysteine and its derivatives[67-70], Co^{II}–selenocysteine[71], Co^{II}–acetylacetone[72], Co^{II}–pyridine[73,74], In^{III}–halide ions[5,8,75-80], In^{III}–NCS^-,[5,77-83] In^{III}–thiourea and its derivatives[6,75,77,79,84], In^{III}–thioacetic and mercaptoacetic acids[77], In^{III}–mercaptoethanol[77], In^{III}–cysteine[84], In^{III}–thiosemicarbazide[56,84], In^{III}–*o*-phenylenediamine[77], In^{III}–2,2′bipyridyl[77], In^{III}–1,10-phenanthroline[77], In^{III}–phthalic acid[75], In^{III}–oxalic acid[77,85-87], In^{III}–tartaric acid[8], In^{III}–acetylacetone[88], Ga^{III}–NCS^-,[89-92] Ga^{III}–halide ions[93], Ga^{III}–N_3^-,[94] Ga^{III}–salicylic and aminosalicylic acids[92], Ga^{III}–methylthiourea[92], Ga^{III}–2-amino-4-hydroxythiazole[92], Ga^{III}–2-amino-4-methyl-5-thiocyanothiazole[92], Sn^{IV}–cysteine[95], Ti^{IV}–NCS^-,[11,17,96-100] Ti^{III}–NCS^- (anodic process),[11] Ti^{IV}–SO_4^{2-},[101,102] Ti^{IV}–F^-,[103] Ti^{IV}–citric acid[15,104], Ti^{IV}–polyphenols[16,104-106], Ti^{IV}–salicylic and sulphosalicylic acids[16,104,105], Ti^{IV}–oxalic acid[104], Ti^{IV}–pyrocatechol[107], Ge^{IV}–polyphenols and their derivatives[108-114], Ge^{IV}–polyhydroxyanthraquinones[113,115], Ge^{IV}–hydroxyflavones[113,116].

III. KINETICS AND MECHANISM OF THE PROCESSES

As in the catalytic liberation of hydrogen[117], the formation of PAC may take place either in the body of the solution (bulk currents; we will thus refer to processes with a reaction layer much thicker than the diffusion part of the electrical double layer[11,15,16,28,66,100]), or with participation of the adsorbed ligand-catalyst (heterogeneous or surface processes)[1,2,35,43-51,62,77-87].

It must be borne in mind that the effect of certain anions and surface-active agents can be linked not only with the surface nature of prewaves, but also with the formation in the solution of new complexes[36-38,51]. Therefore in the present instance it is more important to study the effect of the nature and concentration of the background cation[35,47-50], especially in using alkali metal cations which differ in surface activity[118] but at the same time hardly produce a block-effect and are sufficiently inert to complex formation.

Unlike the catalytic wave of hydrogen with participation of an adsorbed catalyst[119], the temperature coefficient of the limiting current in the heterogeneous reaction for the formation of a PAC is usually sufficiently high (predominance of chemical kinetics)[2,28,35,55,77] but a lower temperature coefficient has also been observed[114] (predominance of the adsorption effect).

The regeneration of a ligand at an electrode is often due to rapid decomposition of the product from the reduction of PAC in the form of the corresponding zerovalent complex[120]. Although extremely unstable zerovalent complexes are usually formed, the difference in the magnitudes of the calculated halfwave potentials of the aquo-ions from a single metal in the presence of different catalytically active ligands[121] allowed the difference in the rate of deactivation of an amalgam[121], or more precisely, in the rate of decomposition of the corresponding zerovalent complexes, to be found. Thus the rates of decomposition of the zerovalent complexes of nickel were found to increase in the following sequence of ligands: pyridine < imidazole < NCS^-.[121]

In many instances the shift in the reduction or oxidation potentials of the PAC is due to the very stable primary hydration of the corresponding aquo-ions of the metals and the weakening (labilisation) under the influence of the ligand of the bonding of the metal ion with the water molecules which remain in the first hydration shell[43,52,122,123]. This conclusion is confirmed by studies[124,125] in which the labilisation of water molecules in a complex was observed with the aid of non-electrochemical methods. For some aquo-ions of metals (for example, Ni^{2+}) which form prewaves, hydration is so strong that in solutions with a high concentration of supporting electrolyte, owing to the marked reduction in the concentration of the aquo-ions of

the metal in the near-electrode layer (the ψ_1-effect[126,127]) a kinetic current was observed: kinetic limitation of the dehydration step[128].

When a PAC is formed in the adsorbed layer, then an electric field evidently exerts a considerable effect on the acceleration of the dehydration[129,130]. It cannot be ruled out that in certain instances the acceleration of the electron transfer stage is linked with the fact that the adsorbed ligand entering into the PAC plays the part of an "electron bridge"[4,131,132]. Attention must be paid to the special state of the adsorbed ligand entering the PAC; it is not impossible that coordination with mercury and with the reacting ion of the metal is effected simultaneously[41,73,133,134]. Some investigators[131,132] pay more attention to the "electron bridge" than to complex formation, although we do not think it very expedient to regard these phenomena as mutually exclusive.

Observations which indirectly characterise the chemical nature of the slow step of the electrode process are of great interest: (1) the steric effect of the ligand (In^{III}–thiourea and its derivatives[84]; Ni^{II}–pyridine and its derivatives[39,39a]). A similar effect was noted in certain complex formation reactions by use of non-electrochemical methods[135]; (2) the relation of the catalytic effect to the structure of isomeric ligands (Ni^{II}–isomers of phenylenediamine[44,45,51]); (3) the inhibition of the catalytic process in the Ni^{II}–pyridine (or its derivatives) systems when the solution is acidified[2,35,39,39a], which is also characteristic for the corresponding non-electrode reactions in complex formation (protonation of the ligand); (4) the inhibition of the catalytic process in the Ni^{II}–thiourea[59] and Ge^{IV}–polyphenol[111] systems on the addition of oxalic, citric, or tartaric acids, in the Ni^{II}–thiourea[36-38], Ni^{II}–pyridine[36-38], Co^{II}–ethylenediamine[66] systems on addition of SO_4^{2-} ions, in the Ni^{II}–thiourea[59] system on addition of NH_3 and Trilon B and the acceleration of the catalytic process under the influence of AcO^- ions (Ni^{II}–pyridine[2,37,38], Ni^{II}–thiourea[37,38], and Ni^{II}–*o*- and *p*-phenylenediamine[51] and N_3^- ions (Ni^{II}–*o*- and *p*-phenylenediamine[51]). Similar effects were also observed in a study of the kinetics of ordinary (non-electrode) complex formation reactions[136-138]; (5) the faster catalytic process in the Co^{II}–pyridine system[74] in comparison with the Ni^{II}–pyridine system[35], which correlates with the kinetics of non-electrode complex formation reactions of particular metal aquo-ions[135].

The bulk catalytic current simplest in mechanism was evidently observed in the Ti^{IV}–NCS^- system[11,96,100]. By use of Koutecky's equation[139,140]:

$$\frac{\bar{i}_k}{\bar{i}_d - \bar{i}_k} = 0.886 \cdot \left(\frac{k_1 \cdot t_1}{K_1'}\right)^{1/2} \cdot c_{NCS^-} \qquad (1)$$

(where $\bar{i}_k$ and $\bar{i}_d$ are the limiting currents, catalytic and diffusion respectively; k_1 and K_1' are the formation rate constant and instability constant of the PAC respectively); it was shown[11,96,100] that the electrode process can be described by the following scheme:

$$Ti^{IV} \xrightarrow[\text{diff.}]{} Ti^{IV} \xrightarrow[k_1]{NCS^-} [Ti^{IV}(NCS^-)] \xrightarrow[\text{red.}]{} \cdot \qquad (2)$$

For simplicity, in scheme (2) and below we do not show the stage of regeneration of the ligand at the electrode and the diffusion noted relates to the transfer of the substance from the depth of the solution to the surface of the electrode (the PAC concentration in the body of the solution is insignificant[141]).

The rate constants for the formation of PAC (scheme 2) calculated by Eqn. (1), are given in Table 1. In addition, Tribalat and Delafosse[11] found the rate constant for the formation of another PAC, $[Ti^{III}(NCS^-)]$, from the anodic catalytic prewave, $k \cong 10^6$ litre mole^{-1} s^{-1} (0.55 M HCl; 21°C).

Table 1. Rate constants for the formation of the complex $[Ti^{IV}(NCS^-)]$ in $HClO_4$ solution at 25°C.

c_{HClO_4}, M	$10^{-3}k_1$, litre mole^{-1} s^{-1}	c_{HClO_4}, M	$10^{-3}k_1$, litre mole^{-1} s^{-1}
0.024	13.0	0.51	6.5
0.044	7.9	0.55*	6±2*
0.10	7.3	1.05	4.8
0.51	6.5	2.0	5.2

*HCl[21°][11]

The catalytic prewaves of Ti^{IV} in the presence of pyrocatechol (H_2Ph), pyrogallol (H_3Pg), citric acid (H_4Cit), and sulphosalicylic acid (H_2Ssal^-) in acid solutions ($HClO_4$) also had a bulk nature[15,16]. The PAC in these systems, with the exception of H_2Ssal^- are formed with the participation in the reactions of electrically neutral ligands, with the release (including H_2Ssal^-) of hydrogen ions[15,16]. Like the catalytic systems with Ge^{IV},[113] Ti^{IV} ions form both PAC and polarographically inactive complexes with these ligands[15,16]. As the concentration was increased, the accumulation of the inactive complexes inhibited the electrode process[15,16]. If it is assumed that the stability of the PAC of Ti^{IV} correlates with the stability of the corresponding polarographically inactive chelates, the rate of formation of the PAC correlates with their stability: $H_2Ph < H_3Pg < H_2Ssal^- < H_4Cit$.[16]

Since the first investigation[142] the effect of ClO_3^- (BrO_3^-) ions on the polarographic wave of Ti^{IV} complexes has been investigated repeatedly, but as found earlier[142], under conditions when there is a large excess of the ligand, whereas in the absence of ClO_3^- ions the prewave was reached along the height of the diffusion wave of the Ti^{IV}. The effect of ClO_3^- ions was first studied at a low concentration of the ligand (NCS^-, H_2Ph, H_3Pg, H_4Cit, H_2Ssal^-), that is, under conditions where there is a double catalytic effect on the process: by the ligand and ClO_3^- ions. An increase in the catalytic prewave of Ti^{IV} complexes with increase in $C_{ClO_3^-}$ (maximally by 5–7 times in comparison with the initial prewave) has been observed[15-17]. A similar comparatively small increase in the limiting current was explained (in greatest detail for the NCS^- ions[17]) on the basis of the following scheme for the electrode process:

$$Ti^{IV} \xrightarrow{NCS^-} [Ti^{IV}(NCS^-)] \xrightarrow[(I)]{\bar{e}} [Ti^{III}(NCS^-)] \xrightarrow{(II)} Ti^{III} + NCS^- \qquad (3)$$

(IV) ↑ (III) ↑ ClO_3^-

ClO_3^-: (V)

by assuming that there are parallel reactions for the oxidation of $[Ti^{III}(NCS^-)]$: to PAC (stage III) and to the initial Ti^{IV} (stage IV). The latter, like stage V, makes little contribution to the increase in current, since it is followed by the slow stage (I).

Another example of bulk catalytic prewaves was observed in the Ni^{2+}–NCS^- system (first prewave)[12,28].

This prewave corresponds to an electrode process with two successive rate-determining chemical stages[12,28]

$$\begin{array}{ccccccc} Ni^{2+} & \xrightarrow[(I,\ k_1)]{NCS^-} & [Ni(NCS)]^+ & \xrightarrow[(II,\ k_2)]{NCS^-} & [Ni(NCS)_2] & \xrightarrow{red.} & \\ \uparrow\downarrow diff. & & \uparrow\downarrow diff. & & & & \\ Ni^{2+} & \rightleftarrows^{NCS^-} & [Ni(NCS)]^+ & & & & \end{array} \quad (4)$$

The kinetic equation for a similar electrode process was first obtained in studies[12,143] by the present author and by Tanaka and coworkers but verified experimentally only in other investigations[12,28]; this became especially convenient after appropriate transformations and the development of a graphical solution of the equations obtained[144]: ($c_{NCS^-} \gg c_{Ni^{2+}}$):

$$y = \frac{\bar{i}_d - \bar{i}_k}{\bar{i}_k} \cdot c_{NCS^-}^2 + 1.13 \left(\frac{K_1'}{k_1 t_1}\right)^{1/3} \cdot \frac{\bar{i}_d}{\bar{i}_k} \cdot \frac{c_{NCS^-}^2}{K_1' + c_{NCS^-}} = A + B \cdot c_{NCS^-} \quad (5)$$

where K_1' is the instability constant of the complex $[Ni(NCS^-)]^+$ and A and B are constants:

$$A = 1.13 \cdot K_1' \cdot \left(\frac{K_2'}{k_2 \cdot t_1}\right)^{1/3}, \quad (6)$$

$$B = 1.13 \left[\left(\frac{K_1'}{k_1 \cdot t_1}\right)^{1/3} + \left(\frac{K_2'}{k_2 \cdot t_1}\right)^{1/3}\right]. \quad (7)$$

K_2' is the consecutive instability constant of the complex $[Ni(NCS)_2]$.

When in scheme (4) the diffusion of the second species (the complex) from the depth of the solution can be neglected Eqn. (5) is greatly simplified even when there are still two successive rate-determining stages[145-147].

The rate constants k_1 and k_2 (Table 2) were found[28] by graphical solution on the basis of Eqn. (5) (in the first paper[12] an inaccuracy was introduced in finding k_1 and k_2, since no allowance was made for the distortion of the limiting diffusion current of Ni^{2+} at high concentrations of the supporting electrolyte[128]). The most important conclusion from the results in Table 2 is the similarity between the rate constants obtained from catalytic currents and those found[148] by a non-electrolytic (flow) method (k_1 = 5.6×10^3 litre mole^{-1} s^{-1}; 25°C; ionic strength 0.5). In addition, it is noteworthy that on the basis of the variations in $E_{\frac{1}{2}}$ and c_{NCS^-},[7,31] and also by a potentiostatic method[149], the reduction of the complex $[Ni(NCS)_2]$ in the Ni^{2+}–NCS^- system has been demonstrated, which agrees with the results discussed above.

Table 2. Rate constants for the formation of the complexes $[Ni(NCS)]^+$ (k_1) and $[Ni(NCS)_2]$ (k_2) at 25°C.

Ionic strength KNO_3 + KNCS	$10^3 k_1$, litre mole^{-1} s^{-1}	$10^{-4} k_2$, litre mole^{-1} s^{-1}	Ionic strength KNO_3 + KNCS	$10^3 k_1$, litre mole^{-1} s^{-1}	$10^{-4} k_2$, litre mole^{-1} s^{-1}
0.05	6.5±1.5	4.2±0.4	0.15	3.0±1.0	2.1±0.3
0.075	4.5±0.5	3.1±0.1	0.20	3.0±1.0	1.9±0.3
0.1	5.0±1.0	2.1±0.1			

Since $c_{Ni^{2+}} > c_{Ni(NCS)^+}$, as c_{NCS^-} is reduced, stage (I) in scheme (4) approaches equilibrium[27,29]:

$$\begin{array}{ccccccc} Ni^{2+} & \rightleftarrows^{NCS^-} & [Ni(NCS)]^+ & \xrightarrow[k_2]{NCS^-} & [Ni(NCS)_2] & \xrightarrow{redn.} & \\ \uparrow\downarrow diff. & & \uparrow\downarrow diff. & & & & \\ Ni^{2+} & \rightleftarrows^{NCS^-} & [Ni(NCS)]^+ & & & & \end{array} \quad (8)$$

The kinetic equation for such a process was first considered in studies[150,151] of dicarboxylic acids, and then in an investigation of metal complexes[143]:

$$\frac{\bar{i}_k \cdot (K_1' + c_{NCS^-})}{(\bar{i}_d - \bar{i}_k) \cdot c_{NCS^+}} = 0.886 \cdot \left(\frac{k_2 \cdot t_1}{K_2'}\right)^{1/3} \cdot c_{NCS^-}. \quad (9)$$

It has been shown theoretically[29] that conversion of scheme (4) into scheme (8) is possible at $c_{NCS^-} \ll 0.1$ M ($c_{NCS^-} \gg c_{Ni^{2+}}$); this conclusion has been confirmed experimentally[29] at $c_{NCS^-} \leqslant 1.5 \times 10^{-2}$ M. Although there is no single opinion about the bulk nature of the catalytic prewaves in the Co^{II}–cysteine (or its derivatives) systems[67-70] it is worth noting the relation[68]:

$$\bar{i}_k = k \cdot c_{Co^{II}}^{1/3} \quad (10)$$

characteristic for a bulk process[70,152] under the conditions c_L = const, $c_{CoII} \gg c_L$ (L is the ethyl ester of cysteine) and the high stability of the PAC:[68]

$$Co^{II} \xrightarrow{diff.} CoII \underset{k_1}{\overset{L}{\rightleftarrows}} [Co^{II}(L)] \xrightarrow{redn.} \quad (11)$$

Since $c_{CoII} \gg c_{CoII(L)}$, the effect of the diffusion of the PAC from the depth of the solution can be neglected. k_1 = $(3.7-4.3) \times 10^3$ litre mole^{-1} s^{-1}.[68]

The following bulk reactions correspond to the anodic catalytic process in the Co^{2+}–ethylenediamine(En) ($NaClO_4$) system[66]:

$$\begin{array}{ccccccc} Co^{2+} & \overset{En}{\rightleftarrows} & [Co(En)]^{2+} & \overset{En}{\rightleftarrows} & [Co(En)_2]^{2+} & \overset{En}{\underset{k_3}{\rightleftarrows}} & [Co(En)_3]^{2+} \xrightarrow{oxn.} \\ \uparrow\downarrow diff. & & \uparrow\downarrow diff. & & \uparrow\downarrow diff. & & \\ Co^{2+} & \overset{En}{\rightleftarrows} & [Co(En)]^{2+} & \overset{En}{\rightleftarrows} & [Co(En)_2]^{2+} & & \end{array} \quad (12)$$

and are describable by the kinetic equation[66,153,154]:

$$\frac{\bar{i}_k}{\bar{i}_d - \bar{i}_k} = 0.886 \cdot \left(\frac{k_3 \cdot t_1}{K_3'}\right)^{1/3} \cdot \frac{c_{En}^3}{K_1' \cdot K_2' + K_2' \cdot c_{En} + c_{En}^2}, \quad (13)$$

where K_1, K_2', and K_3' are the consecutive instability constants of $[Co(En)]^{2+}$, $[Co(En)_2]^{2+}$, and $[Co(En)_3]^{2+}$ respectively. $k_3 = 1.85 \times 10^7$ litre mole^{-1} s^{-1}.[66]

A more complex electrode process is associated with the chemical reactions for the formation of PAC in an adsorbed layer (heterogeneous reactions).

The idea of parallel heterogeneous reactions has been formulated[35,58,74,80]:

$$\begin{array}{ccccccc} M & \xrightarrow{diff.} & M & \xrightarrow[(I,\ \bar{k}_1)]{L_{ads.}} & [M(L_{ads.})] & \xrightarrow{redn.} & \\ L\downarrow\uparrow & & L\downarrow\uparrow & & & & \\ [M(L)] & \xrightarrow{diff.} & [M(L)] & \xrightarrow[(II,\ \bar{k}_2)]{L_{ads.}} & [M(L)(L_{ads.})] & \xrightarrow{redn.} & \\ & & L\downarrow\uparrow & & & & \\ & & [M(L)_2] & \xrightarrow[(III,\ \bar{k}_3)]{L_{ads.}} & [M(L)_2(L_{ads.})] & \xrightarrow{redn.} & \\ & & etc. & & etc. & & \end{array} \quad (14)$$

These obviously most completely characterise such catalytic processes. In scheme (14) (the charges of the species are omitted) M denotes the aquo-ions of the metal, L the ligand, [M(L)], $[M(L)_2]$, etc. are complexes in the bulk of the solution, and $[M(L_{ads})]$, $[M(L)(L_{ads})]$, $[M(L)_2(L_{ads})]$, etc. are PAC.

Since surface catalytic prewaves arise most frequently in solutions which contain complexes with a low stability (K_1' not below 10^{-3}–10^{-4}), in scheme (14) the diffusion of only two species from the depth of the solution to the electrode is taken into account: M and M(L). Despite the low stability of the complex [M(L)] and higher complexes, their participation in the electrode reactions for the formation of PAC cannot be neglected in general, since the bulk rate of formation–dissociation of [M(L)], $[M(L)_2]$, etc. can be rather high. In systems which form

complexes which are more stable in the bulk solution a larger number of heterogeneous parallel reactions must be considered[80] and in systems with bulk complexes of lower stability a smaller number of reactions[35,58,74] or even only a single first (I) reaction[43-51].

Owing to the presence in the PAC (scheme 14) of a ligand adsorbed on the mercury or coordinated with the mercury, similar PAC should (as shown above) differ considerably in electrochemical properties from complexes of formally analogous composition adsorbed from bulk solution[41]. The latter are not reduced at prewave potentials[41].

Irrespective of the reduction of the various PAC in scheme (14) at similar potentials (single prewave)[74,79] or at distinguishable potentials (several prewaves)[35,58], we will examine below only the equation for the overall limiting catalytic current.

Assuming in scheme (14) that the bulk reactions of formation and dissociation of complexes are near a state of equilibrium[29,35,58,59]; that the diffusion coefficients of all the species are similar; and allowing for the effect of the electrical double layer structure on the rate of heterogeneous[117,126,155,156] electron transfer steps which are sufficiently rapid in the region of the limiting catalytic current, the following kinetic equation was found[35,80] for scheme (14) (the coefficient 0.81 has been replaced[140] by 0.886):

$$\frac{\bar{i}_k(K_1'+c_L)}{(\bar{i}_d-\bar{i}_k)\cdot\Gamma_L}=0.886\cdot 10^3\cdot\left(\frac{t_1}{D}\right)^{1/6}\left\{\bar{k}_1\cdot K_1'\cdot\exp.\left(-\frac{z\cdot F}{RT}\psi_1\right)+\right.$$
$$\left.+\bar{k}_2 c_L\cdot\exp.\left(-\frac{z_1\cdot F}{RT}\psi_1\right)+\frac{\bar{k}_3}{K_2'}c_L^2\cdot\exp\left(-\frac{z_2F}{RT}\psi_1\right)+\ \ldots\right\} \quad (15)$$

where K_1' and K_2' are the successive instability constants of the bulk complexes, M(L) and M(L)$_2$ respectively; $\bar{k}_1$, $\bar{k}_2$, $\bar{k}_3$, etc. are the rate constants of the parallel heterogeneous reactions (litre mole^{-1} s^{-1}); Γ_L the surface concentration (mole cm^{-2}) of the adsorbed ligand (the existence of an adsorption equilibrium to a first approximation is assumed); for a dropping electrode this assumption is valid only up to a definite lower level c_L, for example, for *o*-phenylenediamine up to $c_L = 1\times10^{-4}$;[46,50] z, z_1, z_2, etc. are the charges of M, [M(L)], [M(L)$_2$], etc., ψ_1 a potential close to that of the Helmholtz outer layer, the value of which has been given[157] for a supporting electrolyte that is not adsorbed; the effect on ψ_1 the potential of the reacting species of their low concentration can often be neglected (the effect of adsorbed thiourea on the ψ_1 potential has been taken into account[55]); c_L the equilibrium ligand concentration (M) at the boundary between the diffusion layer and the diffusion part of the electrical double layer (c_L is close to the total concentration of the ligand; this is also true for a small excess of ligand L, owing to the regeneration of the ligand at the electrode[144]).

Since catalytic currents are usually investigated in the range of very low c_L, Γ_L can be expressed with the aid of the Henry adsorption isotherm[158]:

$$\Gamma_L=10^{-3}K_L\cdot c_L f_z\cdot\exp\left(-\frac{p\cdot F}{RT}\psi_1\right) \quad (16)$$

where K_L is the adsorption coefficient (cm) and ρ the charge of the ligand.

From (15) and (16):

$$y=\frac{\bar{i}_k(K_1'+c_L)}{(\bar{i}_d-\bar{i}_k)\cdot c_L}=0.886\cdot\left(\frac{t_1}{D}\right)^{1/6}\cdot K_L f_z\left\{\bar{k}_1\cdot K_1'\cdot\exp.\left[-\frac{(z+p)F}{RT}\psi_1\right]+\right.$$
$$\left.+\bar{k}_2\cdot c_L\cdot\exp\left[-\frac{(z_1+p)F}{RT}\cdot\psi_1\right]+\frac{\bar{k}_3}{K_2'}\cdot c_L^2\cdot\exp\left[-\frac{(z_2+p)F}{RT}\psi_1\right]+\ \cdots\right\} \quad (17)$$

At ψ_1 = const, Eqn. (17) becomes

$$y=a+b\cdot c_L+dc_L^2+\ \ldots \quad (18)$$

where a, b, and d are constants, which are conveniently determined by a graphical method[80].

By use of Eqn. (18) we showed[80] the presence of three parallel heterogeneous reactions in the In^{III}–NCS^- system—scheme (14), I, II, and III. An analysis of the variation of the surface activity of $NCS^-_{ads.}$ ions (see below) with the potential in concentrated NaNCS solution showed[83] that in this system the heterogeneous catalytic reaction

$$In^{III}\xrightarrow{2NCS^-_{ads.}}[In^{III}(NCS^-_{ads})_2]\xrightarrow[redn.]{} \quad (19)$$

takes place; it should correspond to a kinetic equation of type (18) at $a = 0$ and $d = 0$, that is, schemes (19) and (14) (without stages I and III) are kinetically indistinguishable. However, as we have shown[80], coefficients a, b, and d in Eqn. (18) are significantly different from zero, which suggests that in this system under our conditions[80] (a very low concentration of NCS^-) all three parallel heterogeneous reactions take place.

For the Ni^{2+}–Py,[35] Co^{2+}–Py,[74] Ni^{2+}–thiourea[58], and In^{III}–I^- [80] systems, in which less stable complexes are formed, Eqn. (18) has been found to be applicable—for the Ni^{2+}–thiourea system, Eqn. (15) at $d = 0$ ($\bar{k}_3 = 0$), that is, in these systems only the two parallel heterogeneous reactions (I) and (II) have a significant effect. It is interesting to note that an analysis of the change in the surface activity of the ions I^-_{ads} with the potential has also shown[132] a smaller stoichiometric number for the I^-_{ads} ions reacting with In^{III} than for NCS^-_{ads}.[83]

The even less stable complex [M(L)] in the Ni^{2+}–*o*-phenylenediamine system[46,47] takes almost no part in the heterogeneous process and the applicability of an equation of type (18) at $b = 0$ and $d = 0$ has been demonstrated[46,47].

In a study[83] of the In^{III}–NCS^- system at a high concentration of NCS^- ions (0.1–6.0 M) the surface activity of the NCS^-_{ads} ions (a_{ads}) was introduced into the kinetic equation instead of Γ_{NCS^-}. It was found from the thermodynamic relation[83,132]:

$$\beta=\frac{a_{ads.}}{a_{soln.}}=\lim_{\Gamma_{NCS^-}\to 0}\frac{\Gamma_{NCS^-}}{a_{soln.}} \quad (20)$$

where a_{soln} is the activity of NCS^- ions in the body of the solution. Hence the quantity βa_{soln} replaces a_{ads} in the kinetic equation:

$$v=k\cdot(\beta\cdot a_{soln.})^x \quad (21)$$

where v is the rate of the process in the region of the limiting current at constant activity coefficient of the transition state, a_M = const and $\psi_1 \simeq$ const (concentrated solution); and x the order of the reaction from the adsorbate. Hence, by use of the variation of β with the potential the applicability of scheme (19) ($x = 2$) was demonstrated[83]. Unfortunately, the accuracy of the dependence of β on the potential, found for concentrated solutions of adsorbate on the basis of model representations is evidently inadequate for the development of this interesting concept. In addition, the postulate of the constancy of the activity coefficient of the transition state—Eqn. (21)—as the potential is varied can hardly be justified[159]. We think that investigations in the range of very low catalyst concentrations, where the Henry adsorption equation applies, is preferable in this respect. It should also be noted that for an electrically neutral ligand (Ni^{2+}–thiourea)[55,58] even

in the range of medium packing it was not necessary to replace Γ_L by a_{ads} in the kinetic equation.

We[35,55] were evidently the first to find—Eqns. (15) and (17)—the rate constants of the heterogeneous electrode reactions for the formation of the PAC (Table 3). The similarity of $\bar{k}_1$ for the various ligands (Table 3), is most probably linked, as for bulk reactions[135], with a common rate-determining stage: the removal of H_2O molecules from the Ni^{2+} aquo-ion. This agrees with the kinetics of bulk reactions[125] and the ratio $\bar{k}_2 > \bar{k}_1$ (Table 3).

The total charge of the reacting species, found on the basis of an analysis of the effect of the ψ_1 potential on the kinetics of the process in the Ni^{2+}–*o*-phenylenediamine system[46,47,50], and consequently the charge of the PAC, was equal to $z + p = +1$, which is explained[46,47,50] by the coadsorption of the anion of the supporting electrolyte (ClO_4^- or NO_3^-) together with the electrically neutral ligand. For the Ni^{2+}–Py system[35,40] at a moderate supporting electrolyte concentration ($\leq$ 0.05 M $NaNO_3$), use of Eqn. (17) showed that $z + p = +2$ and $z_1 + p = +2$. Although coadsorption of the anion of the supporting electrolyte was also observed[160] for Py, the results[35,40] refer to more positive potentials and a lower concentration of supporting electrolyte. For the Co^{2+}–Py system[74], owing to its more negative potential, PAC charges ($z + p$ and $z_1 + p$) also equal to +2 were found on the basis of Eqn. (17) over a wide range of concentrations of the supporting electrolyte. Charges $z + p = +2$ and $z_1 + p = +2$ were similarly found for the PAC in the Ni^{2+}–thiourea system[55,58]. It is interesting to note that in the same system with KI supporting electrolyte[59,60] with considerable adsorption of I^- ions charges $z + p = +2$ and $z_1 + p = +2$ were obtained on using Grahame's values[161] of the ψ_1 potential on the outer layer, which again shows the position of the chemical reaction layer close to the outer surface of the compact part of the electrical double layer.

Table 3. Rate constants for heterogeneous reactions for the formation of polarographically active complexes at 25°C. $NaNO_3$ ($\psi_1 = 0$).

Reaction	$10^{-2}\bar{k}_1$, litre mole^{-1} s^{-1}	$10^{-3}\bar{k}_2$, litre mole^{-1} s^{-1}	Reference
$Ni^{2+} + Py_{ads}$	4.0		35
$[Ni(Py)]^{2+} + Py_{ads}$		1.8	35
$Ni^{2+} + Tm^*_{ads}$	3.8		55

* Thiourea.

Hence the finding by use of Eqns. (15) and (17) for an electrically neutral ligand and doubly charged cation of the expected charges of +2 for the PAC indicates the correctness of the calculation for these reactions of the effect of the electrical double layer under conditions where there are stages with rapid transport of electrons in the range of limiting current.

The complete equation for the catalytic prewave (heterogeneous chemical reaction) with allowance for limitation at the electrochemical stage also is interesting, since this equation, together with an equation of type (17), also allows the charge of the PAC to be found. Such an equation for the simplest process of scheme (14):

$$M^z \xrightarrow{\text{diff.}} M^z \xrightarrow[\bar{k}_1]{L^p_{ads.}} [M(L_{ads.})]^{z+p} \xrightarrow{\text{redn.}} \quad (22)$$

has been obtained[50]. This equation can after simple rearrangements be presented as follows (region of the Henry adsorption isotherm):

$$\frac{\bar{i} \cdot D^{1/2}}{(\bar{i}_d - \bar{i}) \cdot K_L \cdot t_1^{1/2}} \cdot \exp\left[\frac{(z+p) \cdot F}{RT}\psi_1\right] = 0.886 \frac{\bar{k}_1 c_L \cdot k^0_{el} \cdot \exp\left[-\frac{(E-\psi_1)\alpha n_a F}{RT}\right]}{k^0_{el} \cdot \exp\left[-\frac{(E-\psi_1)\alpha n_a F}{RT}\right] + \bar{k}_1} \quad (23)$$

where $\bar{i}$ is the catalytic current at potential E and $\bar{k}_1$ is a rate constant for the reverse reaction (dissociation of PAC).

By choosing the value of $z + p$ in this way, so that the left part of Eqn. (23) reaches a constant value when the negative quantity E is increased, the charge of the PAC is found[50].

For the approximate estimation of the effect of ligand concentration, Eqn. (23) can be simplified by assuming that in the range of potentials of the rise of the prewave from the half-wave potential ($E_{\frac{1}{2}}$) to the potential for the start of the limiting current the quantities ψ_1 and K_L vary slightly. It has been found[162] that under these conditions [Eqn. (31) in Ref. 162]

$$E_{1/2} \simeq 2.3\frac{RT}{\alpha n_a F} \lg 0.886 \cdot \left(\frac{t_1}{D}\right)^{1/2} k^0_{el} + 2.3\frac{RT}{\alpha n_a F} \lg \frac{c_L \cdot K_L}{\bar{K}_1'} + 2.3\frac{RT}{\alpha n_a F} \lg \frac{\bar{i}_d}{\bar{i}_k'} + \psi_1\left[\frac{\alpha n_a - (z+p)}{\alpha n_a}\right], \quad (24)$$

where $\bar{K}_1'$ is the equilibrium constant for the dissociation of the PAC and $\bar{i}_k'$ the limiting current at a potential close to the beginning of the limiting current region.

A complete equation for the surface catalytic prewave, but at the rapid chemical stage of formation of PAC (with allowance for the parallel reaction for the discharge of M^Z ions) has also been given[6,78,84]:

$$\bar{i} = k \cdot \left(\frac{\bar{i}_d - \bar{i}}{\bar{i}_d}\right)\left[(1 - \theta_{cat.}) + \theta_{cat.} \cdot \exp\left(-\frac{\Delta U_{cat.}}{RT}\right)\right] \times \left\{\exp\left[-\frac{(E-\psi_1)\alpha n_a F}{RT}\right]\right\} \cdot \exp\left(-\frac{zF}{RT}\psi_1\right), \quad (26)$$

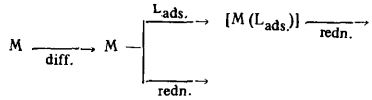
where θ_{cat} is the degree of occupation of the surface of the electrode by the adsorbed catalyst. It may be that in some systems a chemical stage, which greatly reduces the activation energy for the electron transfer (the factor ΔU_{cat}), even in the limiting current region, can take place much more rapidly than the electron transfer stage.

An equation has been obtained[71,163] for the bulk catalytic prewave on the basis of the concept of hypothetical diffusion current. Under the conditions of reduction of only the metal ions in the PAC this equation has the form:

$$\bar{i} = N \cdot \bar{i}_k^d \Big/ \left\{1 + \exp\left[(E - E_{1/2})\frac{\alpha n_a F}{RT}\right]\right\}, \quad (27)$$

where $\bar{i}_k^d$ is the diffusion current of PAC in the absence of a catalytic effect, N the number of metal ions which react in the catalytic cycle with one or more (when there are several ligands in the PAC) species of catalyst ligand. Although Eqn. (27) corresponds to the experimental results[71,163] we think it desirable[164] to use a similar equation [Eqn. (70) in Ref. 117] but with the physically real quantity $\bar{i}_{lim}(i_k)$ instead of the hypothetical diffusion current ($N.\bar{i}_k^d$).

This chapter will be concluded by noting that for the commonly encountered catalytic systems in which electrochemical limitation is almost absent in the region of the limiting current, use of equations of the limiting current type (15) and (17) is preferable. When this is done and an increase in potential results in the superimposition of a parallel process of the discharge of the aquo-ions of the metal, there is the possibility of calculating a corrected value of the limiting catalytic current. For example, for the process



(28)

it was found[40,42] that:

$$(\bar{i}_k)_{corr} = \frac{\bar{i}_d \cdot (\bar{i}_{lim.} - \bar{i}_0)}{\bar{i}_d - \bar{i}_0} \qquad (29)$$

where $\bar{i}_{lim}$ is the observable limiting current and $\bar{i}_0$ the current at the same potential but in the absence of a catalyst.

IV. DETERMINATION OF THE INSTABILITY CONSTANTS OF COMPLEXES

Solution of this problem is facilitated by complexes of low stability usually being formed in the catalytic system itself.

These methods can be divided into two groups: effect of catalytically inactive ions of the metal (method A) and effect of a catalytically inactive ligand (method B).

1. Effect of Metal Ions (Method A)

This method, first proposed by Tribalat[96], is based on the fall in the catalytic current when the catalytically inactive ions of another metal (M′) which bonds the catalyst ligand in a complex [M′(L)] are introduced into the solution. The proportion of the catalyst ligand entering into the complex is easily found from the drop in current and hence the instability constant (K_1') of this complex can be calculated:

$$K_1' = \frac{c_L[c^0_{M'} - (c^0_L - c_L)]}{c^0_L - c_L} \qquad (30)$$

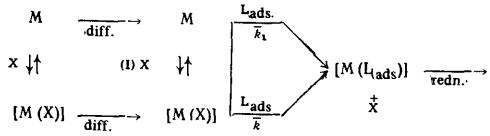
where c^0_L is the total concentration of the ligand (determined from the curve of the catalytic current in the presence of M′ against the total concentration $c^0_{M'}$), and c_L the equilibrium concentration of the ligand (determined from the curve of the catalytic current in the absence of the ions M′). This method was used to determine the instability constants, mainly, of single ligand complexes (K_1'); an excess of M′ ions was used. The results are given in Table 4. The values found for K_1' are close to those obtained by other methods.

2. Effect of the Ligand (Method B)

This direction was first taken by Yatsimirskii and Budarin[165], but they used catalytic systems, which are not discussed in the present review.

Subsequently[36-38] the effect of catalytically inactive ligands on the prewaves of metal ions was investigated and the effects of ligand addition which increase (AcO^-) or decrease (SO_4^{2-}) the currents were used to find the instability constants of the complexes with these ligands[36-38].

Theoretically the solution of this problem was based on the calculation of the parallel process of "religandisation"[36,51,166]. In the simplest example, the entire process can be represented by a scheme proposed simultaneously and independently by Tur'yan and Ruvinskii[36] and by Caja and Mark[51]:



(31)

where X is the polarographically inactive ligand. When $\bar{k} > \bar{k}_1$ the process is accelerated (AcO'); when $\bar{k} < \bar{k}_1$ it is inhibited (SO_4^{2-}).

The equilibrium in stage I (scheme 31) has been characterised[36-38] by use of the same type of kinetic equation as for scheme (14) but with allowance for the parallel reaction of religandisation under conditions different from those of Ref. 166:

$$Z = Z_1 + K_1' \frac{Z_0 - Z}{c^0_X}, \qquad (32)$$

where K_1' is the instability constant of the complex [M(X)], $Z = \bar{i}_k/\bar{i}_d - \bar{i}_k$, Z_L = const at c_Z = const and a constant ionic strength of the solution, $Z_0 = Z$ at $c_{X^0} = 0$, and c_{X^0} is the total concentration of ligand X introduced in an excess in relation to the ions M.

A graphical method was used[36-38] for finding K_1' with the aid of Eqn. (32). The results (Table 4) are close to those obtained by other methods.

V. ANALYTICAL APPLICATION

Catalytically active ligands introduced into a solution in very great excess greatly improve the form of the polarographic wave of a metal and significantly alter the half-wave potential. These advantages are widely used in the polarographic analysis of metals (Ni^{2+}, Co^{2+}, In^{III}, etc.) and have been described in detail in various monographs[168].

A more recent approach considered below is the analytical determination of ligands with the aid of the catalytic prewaves of the metals.

At a low ligand concentration the prewaves were first used[2] for the highly sensitive determination of the ligand (determination of pyridine from the catalytic prewave of Ni^{2+}). The analysis was made with a preliminary calibration graph[44]. Then this method was used for the determination of *o*-phenylenediamine in the presence of a tenfold excess of the *m*- and *p*-isomers (catalytic prewave of Ni^{2+}). With the aim of improving the sensitivity (to 10^{-7} M) it was proposed[45] to use 0.1 M LiI as supporting electrolyte (ψ_1 effect[45,47]). In a further investigation[49] the catalytic prewave of Ni^{2+} in the presence of *o*-phenylenediamine was used for the amperometric titration of *o*-phenylenediamine with the aid of Au^{III} ions. The sensitivity of the determination was 1×10^{-6} M.

The catalytic prewaves of Ti^{IV} in the presence of various ligands have been used[15,16] for the determination of these ligands: citric acid[15], sulphosalicylic acid[16], pyrocatechol[16] and pyrogallol[16]. The additional catalytic effect in the presence of ClO_3^- ions has been used[15,16] to

Table 4. Instability constants (K_1') of complexes, found on the basis of catalytic currents in catalysis by a ligand, 25°C.

Catalytic systems	Supporting electrolyte	Ionic strength	Complex investigated	Method	K_1'	Reference
Ti^{IV}—NCS^-	$HClO_4$	0.70—0.85	$[Co(NCS)]^+$	*A*	$(8.8\pm0.3)\cdot10^{-2}$	96
ditto	ditto	0.50	$[Fe(NCS)]^+$	ditto	$1.5\cdot10^{-2}$	96
»	»	0.6	$[Cr(NCS)]^{2+}$	»	$(5—10)\cdot10^{-4}$	96
»	»	0.7	$[Ni(NCS)]^+$	»	$6.1\cdot10^{-2}$	97
»	»	1.0	ditto	»	$6.7\cdot10^{-2}$	97
»	»	1.5	»	»	$7.6\cdot10^{-2}$	97
»	»	2.5	»	»	$7.7\cdot10^{-2}$	97
»	»	5.0	»	»	$5.4\cdot10^{-2}$	97
»	»	0.62—0.68	»	»	$(4.6\pm0.2)\cdot10^{-2}$*	99
»	»	0.62—0.68	»	»	$(5.7\pm0.2)\cdot10^{-2}$	99
»	»	0.62—0.68	»	»	$(6.7\pm0.4)\cdot10^{-2}$**	99
»	$HClO_4$+ $NaClO_4$	3.0	HNCS	»	5 ± 0.3***	98
Ni^{2+}— NCS^-	KNO_3	1.0	$[Co(NCS)]^+$	»	$(9.0\pm0.4)\cdot10^{-2}$	26
Ni^{2+}— Py	$NaClO_4$	1.0	$[Co(Py)]^{2+}$	»	$(4.4\pm0.4)\cdot10^{-2}$	33
Ni^{2+}— thiourea	$NaNO_3$	2.0	$[Zn(Tm)]^{2+}$	»	0.29 ± 0.01	56
In^{III}— thiourea	$NaClO_4$+$HClO_4$	2.0	$[Zn(Tm)]^{2+}$	»	0.28 ± 0.01	56
Ni^{2+}— thiosemicarbazide (Tc)	$NaNO_3$	2.0	$[Zn(Tc)^{2+}$	»	$(5.1\pm0.1)\cdot10^{-2}$	56
ditto	ditto	1.0	$[Co(Tc)]^{2+}$	»	$(3.9\pm0.1)\cdot10^{-2}$	56
Ni^{2+}— thiourea (Tm)	$NaClO_4$+Na_2SO_4	2.0	$[NiSO_4]$	*B*	$(7.2\pm0.1)\cdot10^{-2}$	36—38
Ni^{2+}— Py	ditto	2.0	ditto	ditto	$(9.6\pm0.1)\cdot10^{-2}$	36—38
ditto	$NaClO_4$+ NaAcO	2.0	$[Ni\,AcO)]^+$	»	0.44 ± 0.01	38
Ni^{2+}— thiourea (Tm)	ditto	2.0	ditto	»	0.36 ± 0.03	38
In^{III}— I^-; In^{III}— — NCS^-	$NaClO_4$+ $HClO_4$	1.1	$InSO_4^+$	»	$(1.0—1.1)\cdot10^{-2}$	167

* 15°C.
** 35°C.
*** Dissociation constants.

increase sensitivity. The sensitivity of the determination of citric and sulphosalicylic acids is ~ 1×10^{-5} M, that for pyrocatechol and pyrogallol is ~ 1×10^{-4} M. The method for the determination of citric acid is considerably faster and simpler than the analytical techniques proposed earlier.

The catalytic prewave of In^{III} has been used[77] for the determination of I^- ions (sensitivity 1×10^{-5} M) and also for the determination[86] of oxalic acid (sensitivity ~ 1×10^{-4} M).

Hence the use of the catalytic prewaves of metal complexes has allowed ligands which are polarographically inactive under ordinary conditions to be determined in several instances.

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Department of Analytical Chemistry,
Krasnodar Polytechnic Institute

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Polarographic Behaviour of Cobalt(II), Nickel(II), and Iron(II)

V.N.Pavlov and V.V.Bondar'

The kinetics and mechanism of reduction of bivalent metals of the iron group at a mercury dropping electrode are examined. The effect of the pH, organic solvent, structure of the double layer, and adsorption of the depolariser on the half-wave potential and limiting currents of the wave for the reduction of cobalt (II), nickel (II), and iron (II) complexes is described. The role of complex formation in depressing the overpotential for the discharge of these metals is considered in detail. Various viewpoints are presented on the mechanism of formation of the catalytic waves of hydrogen, which appear when doubly-charged ions of these metals and various organic substances are present in the solution simultaneously.
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I. INTRODUCTION

Despite many papers dealing with the mechanism of the reduction of ions of metals of the iron group at a mercury dropping electrode (MDE), there is not a sufficiently detailed and systematic review of these studies. We have tried to fill this gap to some extent.

From the point of view of polarography, the most noticeable general feature is that cobalt, nickel, and iron are almost insoluble in mercury, and the redox potentials of these metals are very similar; there is also much in common in the mechanism of the polarographic behaviour of these metals.

In this review we have examined only certain (we think the most important) aspects of the electrochemical release of cobalt, nickel, and iron from their bivalent state at a mercury dropping electrode.

2. EFFECT OF THE pH OF THE SOLUTION ON THE POLAROGRAPHIC BEHAVIOUR OF COBALT, NICKEL, AND IRON

Brdička[1] was the first to observe that $E_{\frac{1}{2}}$ of the cobalt wave is shifted to more negative potentials when the pH of the solution is decreased. A similar relation between the shift in the discharge potential of cobalt or nickel ions and the pH of the solution was found at a solid cobalt electrode[2] and was also noted in earlier studies[3-5].

Since in aqueous solution the cobalt ion exists as a complex with six water molecules, Brdička[1] explained the decrease in the negative values of $E_{\frac{1}{2}}$ of cobalt when the pH of the solution was increased by the partial dehydration of the hexahydrate with the replacement of one water molecule by an OH^- ion:

$$\underset{(I)}{[Co(H_2O)_6]^{2+}} + H_2O \rightleftarrows H^+ + \underset{(II)}{[Co(H_2O)_5OH]^+}. \qquad (1)$$

He thought that such a complex would be reduced more readily than the hexahydrate.

The polarograms of Fig. 1, taken from Brdička's work[1] show clearly how the wave for the reduction of Co^{2+} is displaced to more negative potentials as the solution is acidified, and finally merges with the background. As the result of the selection of definite values of Co^{2+} concentration, pH of the medium, and temperature, in the absence of strong complex-forming substances splitting of the cobalt wave could be observed. Fig. 2[1] shows the appearance and increase of the wave for the reduction of complexes II (reaction 1) as the temperature is raised.

In certain instances the splitting of the wave could not be observed but semilogarithmic plots of the waves for the reduction of Co^{2+} showed inflections[6-8]; the explanation could be that the observed wave really describes two processes in which two types of complex participate—cf. Eqn. (1).

Our results[8] mainly agree with Brdička's observations[1]: as the pH is increased from 2.9 to 4.0 $E_{\frac{1}{2}}$ for Co^{2+} in a solution of 0.1 N KCl + HCl varies from −1.380 to −1.345 V. In the pH range 4.0–4.5 $E_{\frac{1}{2}}$ hardly alters. We were unable to investigate the variation of $E_{\frac{1}{2}}$ with pH for cobalt in the range pH < 2.9 owing to the superimposition of the hydrogen discharge wave on the cobalt wave.

Interestingly, the transfer coefficient (α), determined from the slope of the graph constructed on coordinates of $\lg i$ against E at the potentials of the start of the cobalt wave, also shows a decrease in the rate of the electrochemical process for the reduction of the cobalt ion in the acidic range of pH (< 4.0).[8] Fig. 3 shows the change in α as the pH of the solution is varied.

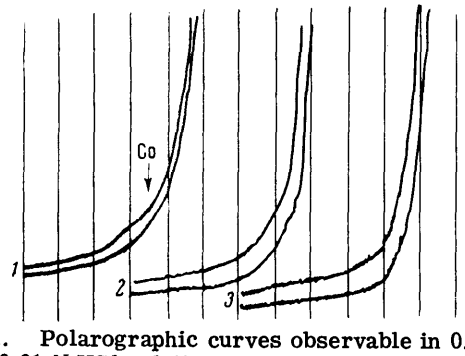


Figure 1. Polarographic curves observable in 0.01 N $CoCl_2$ + 0.01 N KCl solutions at various HCl concentrations: 1) without addition of HCl; 2) 10^{-5} N HCl; 3) 10^{-4} N HCl. The curves start at −0.6 V.

Zytner and Rotinyan[9] used the method of recording electrostatic partial polarisation curves to study the discharge of Co^{2+} ions at a cobalt electrode in 0.6 M cobalt sulphate solution at 56°C in the pH range 2.55–3.80. They found that the cathodic potential for the discharge of cobalt ions shifts in the negative direction as the pH is reduced. The order of the cathodic reaction with respect to Co^{2+} and OH^- ions is 1.1 and 0.9 respectively, that is, close to 1. In explaining the mechanism of the reaction Zytner and Rotinyan[9] started from ideas on the participation of the OH^- ion in a potential-determining stage. Kravtsov and Lokshtanova[10] also noted that in the electrodeposition of cobalt at a cobalt electrode (from 1 N $CoSO_4$ + H_3BO_3) the rate of the process increased as the pH was raised from 3.5 to 4.2, showing that the rate-determining stage of the cathodic process is the transfer of the first electron to Co^{2+}.

An analogous relation between $E_{\frac{1}{2}}$ and pH is also observed for iron[11,12]. $E_{\frac{1}{2}}$ hardly alters as the pH is changed from 4.5 to 5.0 but at pH below 4.5–5.0 it is shifted rather significantly in the negative direction (Fig. 4). However, Dahms[13] did not observe a change in the $E_{\frac{1}{2}}$ of the iron wave.

A variation of $E_{\frac{1}{2}}$ with pH was also noted for all the metals of the iron group in the presence of a complex-forming substance (pyridine).[14]

A variation of $E_{\frac{1}{2}}$ for the nickel ion with the pH at the mercury dropping electrode in the absence of a complex-forming substance could not be observed[23].

At first glance the formation of a complex of a metal with an OH^- ion according to reaction (1) in a solution where the concentration of free hydroxyl ions is negligibly small ($\sim 10^{-11}$–10^{-10} g-ion litre^{-1}) seems improbable. However, allowance must be made for the fact that the process leading to the formation of a complex in which one molecule of water is replaced by a hydroxyl ion is kinetic in nature. Water, the concentration of which is ~ 55 M, participates in this process as a donor of hydroxyl ions. The kinetic nature of the wave for the discharge of the hydroxo-complex is shown by the large temperature coefficient of the limiting current of this wave (cf. Fig. 2). It can also be postulated that the hydroxo-complex is formed as a result of the slow deprotonisation of the hexa-aquo-complex of cobalt.

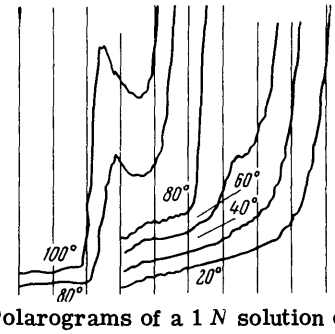


Figure 2. Polarograms of a 1 N solution of $CoCl_2$ at various temperatures. The sensitivity of the galvanometer decreased on going from 60° to 80° and 100°C.

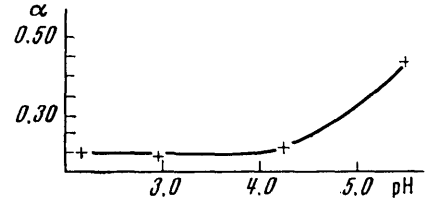


Figure 3. Variation of the transport coefficient α for waves of cobalt (0.64×10^{-3} M) with the pH of 0.1 N KCl + xHCl solution[8].

The decrease in the negative values of the half-wave potential as the pH of the solution is increased evidently reflects the fact that the observable wave is obtained as a result of the superimposition of two waves (the $E_{\frac{1}{2}}$ of which are different), which correspond with the discharge of complexes II (first wave) and I (second wave), according to reaction (1). As the pH is raised there is an increase in the wavelength corresponding to complex II, the $E_{\frac{1}{2}}$ of which is less negative than the $E_{\frac{1}{2}}$ of the hexahydrate wave. This also leads to a shift in the $E_{\frac{1}{2}}$ of the overall wave to less negative values as the pH is raised.

The mixed nature of the waves causes inflections on the curves on the semilogarithmic graphs[6–8] and the lower part of the curve is found by some[1,7,8] to be steeper than the upper, whereas another study[6] shows the lower part of the curve to be the less steep. The differences in the slopes of the initial parts observed by different authors are evidently due to differences in the experimental conditions.

As mentioned above, by choice of the experimental conditions (concentration of the cobalt salt, temperature of the solution, pH) Brdička succeeded in distinguishing the pure wave corresponding to the discharge of complex II (reaction 1). The value of αn_a which we found from the initial part of the graph plotted in coordinates of $\lg i$ against E for this wave is ~ 50 mV. The first wave is appreciably steeper than the main wave. Evidently the process which corresponds to the transfer of an electron to the complex $[Co(OH)(H_2O)_5]^+$ is rather close to reversible under these conditions.

Cosowic and Branica[15] found a charge of $Z = +2$ for the cobalt complex which exists in a phosphate buffer in the presence of 0.5 M $NaClO_4$ and consider the existence of the complex $[Co(OH)(H_2O)_5]^+$ improbable. However, it must be borne in mind that the equilibrium of reaction (1) is evidently shifted to the left, since the wave which corresponds to the reduction of this complex cannot exceed 10 to 20% of the total wave[1,7]; therefore the calculation of the kinetic parameters of the overall wave, despite the existence of a complex with $Z = +1$, can lead to a value of Z close to +2. In addition, as noted by Cosowic and Branica[15] they have been investigated only in a narrow range of pH (6.5–8.14).

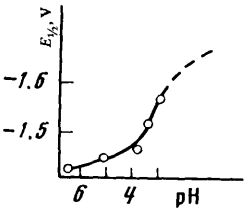


Figure 4. Variation of $E_{\frac{1}{2}}$ for the Fe^{II} reduction wave with the pH. [11]

We have calculated the number Z from Turyan's results[6] with the aid of an equation taken from Mairanovskii[16]:

$$\Delta E_{1/2} = \Delta\psi_1 \frac{\alpha n_a - Z}{\alpha n_a}, \quad (2)$$

where Z is the charge of the species participating in the electrochemical reaction, α the transfer coefficient, n the number of electrons which is transferred in the potential-determining stages, and $\Delta\psi_1$ the potential jump in the diffusion part of the double layer. For a solution[6] of cobalt in 0.04–0.1 M Na_2SO_4 $Z = +1.25$, which evidently reflects the mixed nature of the wave in which both species with charge +1 and species with charge +2 participate.

We think it unusual that a species with one positive charge less should be discharged more readily than an analogous species carrying two positive charges. However, such a phenomenon is also observed when the concentration of the chlorides is increased (see below), when species with a smaller positive or even a negative charge are formed from a hexahydrate with charge +2. The drop in polarisation when water molecules are replaced by a hydroxyl ion is evidently due to several reasons. One of them, discussed below in most detail, is the acceleration of the dehydration on the introduction into the inner coordination sphere of a foreign ligand. In addition, it is necessary to take into account that the presence of an OH^- ion in the composition of a complex firstly allows the reaction centre of the complex—the metal ion—to approach nearer the surface, since the OH^- ion is smaller than H_2O; secondly, the transfer of one electron to the M^{2+} ion using the "relay" nature of the transfer (the OH^- ion transfers its electron to a metal ion, exchanging one electron with the electrode surface). It must be taken into account that a non-symmetric coordination sphere is deformed more readily (with subsequent dehydration) in the field of the double layer than is a symmetric one consisting of six water molecules.

3. ROLE OF COMPLEX FORMATION

Cobalt(II) and nickel(II) are known to exist in an aqueous solution in the absence of other complex-forming agents as the hexahydrates which have a stable octahedral configuration[17]. It has been shown recently[18] that iron(II) exists in aqueous solution also in the form of the hexahydrate. Such a structure for the complex is one of the reasons for the high overpotential of the reduction of the ions of the metals of the iron group. However, only the hydrate of the doubly-charged metal ion is stable in aqueous solution. The complex of the singly-charged ion, which should be formed after the transfer of the first electron (see, for example, Molodov and Losev[19]) in aqueous solutions of perchlorates, sulphates, nitrates, and other anions which do not form stable complexes with this ion, is unstable and immediately acquires a second electron; therefore in aqueous solutions the salts of these ions of cobalt, nickel, and iron give one two-electron (irreversible) wave with diffusion control[6-8,17,20].

According to Gierst and Hurwitz[21-24] the hexahydrate complexes of nickel and cobalt are partly dehydrated before the electrode reaction proper. The rate constant of the dehydration increases with the negative values of the ψ_1-potential (discussed in more detail below).

Attempts were made to determine the number of water molecules detached in stages which precede the transfer of electrons[25,26]. The polarographic curves were used to determine the activation energy of the dehydration of nickel hexahydrate[5,25], the value of which agrees satisfactorily with the activation energy of the isotopic exchange of one molecule of water between the solvent and the first sphere of hydration of nickel hexahydrate, determined by the NMR method[27] to be 11.6 kcal $mole^{-1}$. Hence it is concluded that in the stage which precedes the transfer of electrons into $NaClO_4$ solutions either one water molecule is detached[25] or another molecule of water[26] is introduced into the inner coordination sphere. In either instance the complex loses the stable octahedral configuration, which facilitates the deformation of the inner sphere and the transfer of an electron to the central atom.

The number of waves on the polarogram and their position on the potential axis depends on the nature and concentration of the ligand. The complex-forming substances, which give extremely stable complexes with our metals, for example, various compounds which contain $-NH_2$ or $\geqslant NH$ groups[28], have a greater tendency to form two waves. Halide ions are weaker complex-forming substances than amines; therefore they bring about only a decrease in $E_{\frac{1}{2}}$.

A similar effect was observed on raising the concentration of LiCl or LiBr (from 1 to 20 M) in a cobalt,

nickel, or iron solution [30,31], on increasing the concentration of calcium chloride in a solution of iron salt, and also in the partial replacement of saturated calcium perchlorate solution by calcium chloride in a solution of cobalt, nickel, or iron salts [11,31,32]; increasing the chloride concentration to 0.25 M reduces the half-wave potential of cobalt from −0.9 to −0.7 V. The graph in Fig. 5, constructed from Aylward and coworkers' results [30], shows the variation of $E_{\frac{1}{2}}$ for cobalt with the lithium chloride and bromide concentrations. It is necessary to bear in mind that when there is a considerable increase in the concentration of electrolytes such as lithium [30] or calcium [31] halides an additional shift in $E_{\frac{1}{2}}$ for the waves of the hydrated metal ions can appear due to the dehydrating action at high concentrations of the supporting electrolytes. Since there are six water molecules in the inner coordination sphere of complexes of iron group metals and another 26 molecules in the second sphere (the heat of formation of the second sphere is 240 kcal g-ion^{-1}—almost equal to the heat of formation of the first sphere) [18], the introduction, for example, of electrolytes such as LiCl and $CaCl_2$ [30,31] should lead to an acceleration of the dehydration of the hexahydrate and consequently to a shift of $E_{\frac{1}{2}}$ to less negative potentials.

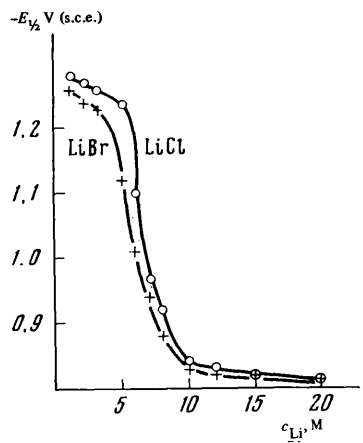


Figure 5. Variation of $E_{\frac{1}{2}}$ of the cobalt wave with the molal concentration of lithium chloride and bromide. [30]

When the concentration of halide ions is increased there is a gradual conversion of the octahedral hexahydrate into the tetrahedral tetrahalide [18,30]. For example, in LiCl and LiBr the transitional region corresponds to 8–14 M. The change from hexahydrate to tetrahalide affects the form of the polarogram: a graph constructed in semilogarithmic coordinates consists of two straight-line portions, the lower of which is the steeper [30]. A CN^- ion in a solution of nickel salt also forms (when its concentration is increased) a doubly-charged complex of tetrahedral structure $[Ni(CN)_4]^{2-}$. [33-37]

It is interesting that despite the anionic nature of the MX_4^{2-} complex (where X = Cl, Br, I, CN, or NCS) which exists in sufficiently concentrated solutions, the half-wave potential of the halogeno-complex is less negative than the half-wave potential of the hexahydrate, which has a charge of +2.

When the solution contains a ligand capable of forming a sufficiently stable bond with a metal ion, the water molecule that has been detached in the inner coordination sphere is replaced by a corresponding molecule or ion which is introduced into the inner coordination sphere. The introduction of the foreign ligand increases the rate constant of the exchange (k_{H_2O}) for the subsequent water molecules [27-29]. For example, for $[Ni(H_2O)_6]^{2+}$ $k_{H_2O} = 2.74 \times 10^4$ s^{-1}, [27] and for the complex in which one water molecule is replaced by glycine $[Ni(Glyc)(H_2O)_5]^{2+}$ k_{H_2O} is 1.2×10^5 s^{-1}. [29] Some investigators think [25,29] that the increase in the rate constant for the exchange of the second and subsequent water molecules is the reason for the decrease in the polarisation in the introduction into aqueous solution of a complex-forming substance (leading in certain instances not only to a shift in the main wave but also to the appearance of new waves in a less negative range of potentials).

On reaching a certain concentration of the ligand the half-wave potential of the ionic complex can reach a limiting value and when the concentration of the ligands is increased further it starts to shift to the side of more negative potentials. However, this shift in the negative direction is small, since $E_{\frac{1}{2}}$ usually remains smaller in magnitude than $E_{\frac{1}{2}}$ of the hexahydrate (see Table, which is constructed from results of Refs. 11 and 31). Despite some shift in the negative direction the degree of reversibility is usually unaltered.

Some electrochemical characteristics of the reduction of doubly-charged ions of iron-group metals.

Compn. of the supporting electrolyte	Ni^{2+}			Co^{2+}			Fe^{2+}			Comparison electrode
	$E_{1/2}$	$\Delta E_{1/2}$	α	$E_{1/2}$	$\Delta E_{1/2}$	α	$E_{1/2}$	$\Delta E_{1/2}$	α	
0.1 M $NaClO_4$	−1.09	—	—	−1.22	—	—	−1.33	—	—	s.c.e.
saturated solution of $Ca(ClO_4)_2$	−0.712	0.378	0.43	−0.873	0.347	0.30	−0.981	0.349	0.50	ditto
saturated solution of $Ca(ClO_4)_2$ +0.25 M $CaCl_2$	−0.317	0.773	0.52	−0.674	0.546	0.62	−0.936	0.394	0.71	»
saturated solution of LiCl	−0.410	0.680	1.02	−0.800	0.420	0.88	−1.060	0.270	0.91	»
10N $CaCl_2$	−0.48	—	—	−0.9	—	—	−1.125	—	—	S.C.E.

The limiting current can also depend upon the ligand concentration. Thus, when acetylacetone (HAcac) is added [15] to a 5×10^{-4} M cobalt nitrate solution (in a phosphate buffer + 0.5 M $NaClO_4$) the cobalt wave decreases until the concentration of the free ligand reaches 10^{-4} M. The observed regularity is explained by the competition between the water and acetylacetone. A polarographically inactive complex $CoAcac_2$ is formed. The limiting current is kinetic in nature since the kinetics of formation of $CoAcac^+$ from this complex also determines the height of the wave that is observed [15]:

$$\begin{array}{ccccc} Co(H_2O)_6^{2+} & \rightleftarrows & CoAcac^+ & \rightleftarrows & CoAcac_2 \\ \alpha n_\alpha = 0.8 \downarrow\uparrow & & \downarrow\uparrow \alpha n_\alpha = 1.3 & & \\ Co\,(Hg) & & Co\,(Hg) & & \end{array}$$

For ligands which form stable complexes with the metal ion the dependence of $E_{\frac{1}{2}}$ and the limiting currents

upon the ligand concentration is more complex; a low concentration of the ligand leads to a reconstruction of the hydrate sheath of the ion. The influence of the concentration of diaminopropane[25] on $E_{\frac{1}{2}}$ and the number and form of the nickel waves has been studied in detail[25]. In the range of ligand concentrations where $\lg C_X < -8.1$ (in an acid solution of $NaClO_4 + HClO_4$, $I = 0.5$) a single wave is observed (as in the absence of the ligand), the $E_{\frac{1}{2}}$ of which does not change as the ligand concentration is altered ($E_{\frac{1}{2}} = -1.603$ V). This wave corresponds to the discharge of the hexa-aquo-complex of nickel. In the range $-8.1 < \lg C_X < -7.6$ there are two waves on the polarogram (see Fig. 6), the half-wave potentials of which hardly alter as the concentration of the complex-forming agent is increased. The first wave (that is, the wave at less negative potentials) on the polarogram obtained under the conditions described corresponds to the reduction of the complex with diaminopropane. When the diaminopropane concentration is increased ($\lg C_X > -7.6$) the first wave is displaced to less negative potentials. In the range $\lg C_X > -5.25$ the first wave merges with the second and with a further increase in the ligand concentration this combined wave again starts to shift to more negative potentials.

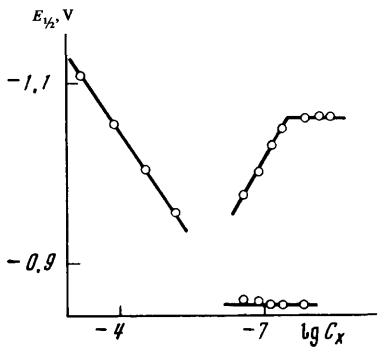


Figure 6. Change in the number of waves and half-wave potentials of nickel ion (1×10^{-4} M) with the logarithm of the ligand concentration (diaminopropane) in a solution of lithium perchlorate[25].

A similar picture is observed in the presence of pyridine. In the polarography of a solution of a nickel salt in the presence of $< 10^{-4}$ M pyridine a single wave with $E_{\frac{1}{2}} = -1.025$ V is observed[38]. An increase in the pyridine concentration by an order of magnitude leads to the appearance of two new waves, the $E_{\frac{1}{2}}$ of which are −0.76 V and −0.86 V respectively. When the pyridine concentration is raised further (to 0.1 M) two of the waves on the polarogram disappear and there remains only the wave observed in the less negative range of potentials; this wave shifts slightly in the negative direction when the pyridine concentration is increased further. Fig. 7, constructed from the results of Kemula and coworkers[38] shows the change in the number of waves and the $E_{\frac{1}{2}}$ of the nickel waves as the pyridine concentration is varied.

However, in several instances only a displacement of the wave along the potential axis is observed. Thus, when a ligand such as the hypophosphite ion ($H_2PO_2^-$) is introduced into a cobalt solution with pH 5.5 only a shift of the wave towards more negative potentials is observed[8].

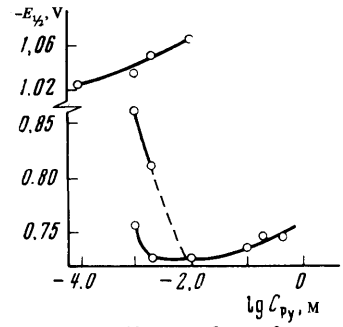


Figure 7. Variation of the number of waves and half-wave potentials in the reduction of a nickel ion with the pyridine concentration[38].

Calculation of the number of hypophosphite ions entering into the complex[8] under the condition that $\alpha = 0.5$ gives a value of 1. The semilogarithmic graph of Fig. 8 shows the change in $E_{\frac{1}{2}}$ of the cobalt wave as the sodium hypophosphite concentration (C_{HPP}) is raised. The curve for a solution with pH 4.5 has an inflection due to the appearance of the polarographic activity of the hypophosphite in a sufficiently acid medium in the presence of cobalt ions[8]; this will be discussed in greater detail below.

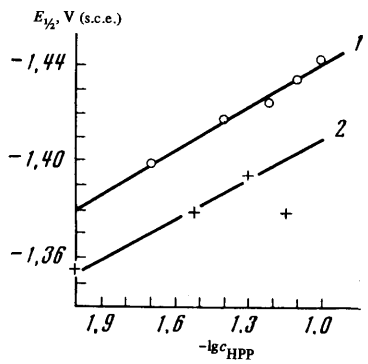


Figure 8. Variation of the half-wave potential of the cobalt ion with the concentration of sodium hypophosphite in solutions with pH 5.5 (curve *1*) and pH 4.25 (curve *2*).[8]

4. INFLUENCE OF ORGANIC SOLVENT

The partial or complete replacement of water by an organic solvent leads to a significant change in the polarographic conditions. On the addition of an organic solvent in a concentration comparable with that of the ion being studied or greater by about an order of magnitude, the organic solvent can be regarded as an ordinary ligand, the introduction of which into the solution leads usually to the

partial dehydration of the hexa-aquo-complex of the metal, and the replacement of even a single water molecule in the inner coordination sphere by a foreign ligand facilitates reduction, that is, leads to a shift in the $E_{\frac{1}{2}}$ of the wave of the complex to more positive potentials. In this nickel shows the greatest tendency towards the formation of complexes, so that $\Delta E_{\frac{1}{2}}$ for nickel ($\Delta E_{\frac{1}{2}} = E_{\frac{1}{2}}^{H_2O} - E_{\frac{1}{2}}^{L}$) has the greatest absolute value. At a higher concentration of the organic solvent [39,40] the polarogram includes a wave having an $E_{\frac{1}{2}}$ several tenths of a volt less negative than the half-wave potential of the hexahydrates of these metals.

Interestingly, the completely solvated ion, like the completely hydrated one, is more difficult to reduce than an ion with a solvate sheath in which there are ligands of two or more kinds. Thus the addition of 8×10^{-4} M xanthate to a 4×10^{-4} M solution of a nickel salt (in a supporting electrolyte of 0.2 M $LiClO_4$) in absolute ethanol shifts $E_{\frac{1}{2}}$ from −0.840 to −0.667 V. [39] In ethanol solution (in the presence of small quantities of 1,10-phenanthroline) the wave corresponding to the transfer of an electron with the formation of a complex of cobalt(I) is irreversible: its $E_{\frac{1}{2}} = -1.02$ V, but when the 1,10-phenanthroline concentration is increased the $E_{\frac{1}{2}}$ is appreciably shifted in the positive direction and the wave acquires a quasireversible nature [40-42].

The introduction into an aqueous solution of an organic solvent capable of the formation of a stable complex, in the presence of other ligands can lead to the appearance of two waves corresponding to complexes of different composition. Thus in 1 M KCNS, taken as supporting electrolyte, nickel gives a single sharp wave with $E_{\frac{1}{2}} = -0.695$ V (s.c.e.), but when acetamide is added there are two waves on the polarogram [43]. The first wave was thought [43] to be due to the reduction of the thiocyanato-complex of the nickel ion, the second wave, which appears at more negative potentials, corresponds to the reduction of the complex of nickel with acetamide. Both waves are irreversible. When the acetamide concentration is increased $E_{\frac{1}{2}}$ of the second nickel wave is shifted monotonically to more negative potentials, from −1.562 V (5% acetamide) to −1.648 V (30% acetamide); there is also an increase in the irreversibility of the electrochemical process.

The opposite behaviour has also been observed [44]: the introduction of an organic solvent (ethanol, ethylene glycol, and especially propanol) leads to the merging of the two waves on the polarogram of nickel in 1–1.5 M solutions of HCOONa, Na_2SO_4, and NaI into a single wave [44].

In anhydrous dimethylformamide (DMF) in the presence of the Cl^- ion nickel also gives two waves [45], the first of which increases as the concentration of Cl^- ion in the solution is increased.

As regards the reversibility of the waves for the reduction of our metals in non-aqueous solvents it is usually considerably higher in comparison with the waves observable in water. Thus it has been noted that the waves of all three metal ions under consideration are reversible in DMF [45]; the cobalt wave is reversible in isobutyronitrile (the slope of the wave is 34 mV, $E_{\frac{1}{2}} = -0.60$ V relative to the s.c.e.) [46], but in this solvent it is not strange that the nickel wave is irreversible, though this has been attributed [46] to the possible presence of traces of water.

Allowance must also be made for the organic solvent exerting a specific action, since when its concentration is increased there is a decrease in the adsorbability of the organic ligands or of the complexes with these ligands, which should lead to an increase in polarisation.

Furthermore, when the concentration of the organic solvent is increased there is a decrease in the dielectric permeability of the medium, in consequence of which the association of our cations with the anions of the indifferent electrolyte is possible.

5. INFLUENCE OF THE STRUCTURE OF THE ELECTRICAL DOUBLE LAYER

In the reduction of cations at a negatively charged surface, the electrostatic action of the field facilitates their approach to the electrode surface [16,47]. On the other hand, on the positively charged surface of the electrode the electrostatic action of the field retards the electrode processes involving the cations and accelerates the processes involving the anions.

The reduction of cobalt, nickel, and iron complexes usually obeys these rules because the complexes of these metals (in a bivalent state) usually have a charge $Z \geqslant 0$ and at the same time the waves of these complexes lie on the negative branch of the electrocapillary curve. An exception is the complex of nickel in solutions of ligands such as Cl^-; for example, $E_{\frac{1}{2}}$ for nickel in a saturated $Ca(ClO_4)_2$ solution +0.25 M in $CaCl_2$ is −0.317 V (s.c.e.). [31]

On the above basis it is easy to explain the fact that when the concentration of the indifferent electrolyte is increased (within certain limits) $E_{\frac{1}{2}}$ for the waves of cobalt, nickel, and iron are shifted to the side of more negative potentials. For example, when the concentration of $CaCl_2$ (taken as supporting electrolyte) is raised to 1 N, the Fe^{2+} wave is shifted by ~ 300 mV in the negative direction. This is accompanied by a decrease in the limiting current, which the investigators attributed to an increase in the viscosity of the solution and a corresponding change in the diffusion coefficient of the iron [48]. A shift in $E_{\frac{1}{2}}$ in a negative direction when the ionic strength is increased is also observed in the reduction of cobalt complexes with cysteine [16] and for the "simple" ions of cobalt [8] and nickel [6].

As regards nickel complexes, the influence of the double layer is somewhat peculiar [49]. The reduction of nickel hexahydrate in dilute solutions is accompanied by the appearance of a single wave [49] with a sharply expressed limiting current plateau. However, as the concentration of the electrolyte is raised the limiting current of the wave falls completely and starts to depend upon the potential [49,50], increasing with increase in the negative potential. At the same time, $E_{\frac{1}{2}}$ for this wave hardly alters (Fig. 9); when the KCl concentration is increased above 0.8 M a second wave also appears, lying in a more negative range of potentials [8]. Splitting of the nickel wave was also observed at high concentrations (1–1.5 M) of sodium formate, sulphate, and iodide, used as supporting electrolyte [44]. In concentrated solutions of the supporting electrolyte the limiting current for the reduction of Ni^{2+} acquires a kinetic nature [49,50], and the magnitude of the kinetic current increases with the cathode potential (cf. Fig. 9). Gierst [21-24] assumes that hydrated nickel ions are partly dehydrated in the field of the double layer before the electrochemical stage proper:

$$[Ni(H_2O)_6]^{2+} \underset{k_b}{\overset{k_f}{\rightleftarrows}} [Ni(H_2O)_x]^{2+} + (6-x)H_2O$$

and the rate of dehydration increases with the absolute magnitude of the negative ψ_1-potential; hence the increase in the limiting current with increase in the cathodic potential is due to an increase in the negative value of the ψ_1-potential. The limiting current for the discharge of nickel

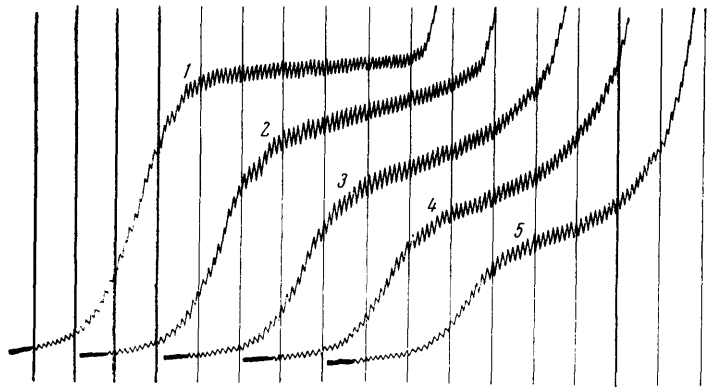


Figure 9. Effect of the concentration of an indifferent electrolyte (NaCl) on the wave for the reduction of 10^{-3} M $NiSO_4$ in the presence of 0.005% gelatin[49]. NaCl concentration, M: 1) 0.1; 2) 0.5; 3) 1.0; 4) 1.5; 5) 2. Each curve starts at −0.7 V (s.c.e.); the distances between the abscissae are 0.2 V.

ions in dilute solutions of an indifferent electrolyte (for example, in 0.1 *N* NaCl) is limited by diffusion, since at low concentrations of the electrolyte the negative value of the ψ_1-potential is so high that the increase in the rate of the preceding reaction brought about by the influence of the double layer has the result that the diffusion of the nickel ionic complex towards the electrode becomes the slowest stage of the process.

Even adsorption of the anion on the mercury surface can occur at a sufficiently high concentration of the indifferent electrolyte. This effect is opposite in sign to the effect of the cation; therefore, for example, when the concentration of chlorides is increased to more than 1–2 M there is a shift in $E_{\frac{1}{2}}$ for iron(II)[48] and cobalt(II)[31] to less negative potentials.

Fig. 10 shows the change in $E_{\frac{1}{2}}$ for iron(II) (curve *1*) as the $CaCl_2$ concentration is varied. Increasing the $CaCl_2$ concentration above 2 *N* shifts $E_{\frac{1}{2}}$ to less negative potentials. However, it is necessary to take into account the complexing action of the anion, which it is difficult to separate from the influence of the double layer during the change in the concentration of the anion[31].

6. INFLUENCE OF THE ADSORPTION OF THE DEPOLARISER

It is also necessary to consider the influence of the adsorption of the complex itself on the kinetics of the electroreduction of the metals concerned. This is especially so in those instances when the ligand is an organic molecule or an organic ion, since organic compounds (especially those which have a sufficiently high molecular weight) are readily adsorbed on the surface of mercury.

Olson[29] observed an increase in the reversibility of the wave for the reduction of the complex of nickel with triethylenetetramine. Since the rate constant for the exchange of the second water molecule is here lower than the rate constant for the exchange of the first water molecule, Olson considers that the reversibility of the wave for the reduction of the complex is due not to the labilisation of the complex but to its specific adsorption at the surface of the electrode. In this instance the reaction centre of the complex is located in the inner Helmholtz plane, where there is a much higher potential gradient, as a result of which the reduction is facilitated.

The influence of the adsorption of pyridine, thiourea[51–53], and diaminopropane[25] on the nickel wave, and of 2,2′-bipyridyl on the cobalt and iron waves[54] has also been noted. Results on the influence of adsorption of complexes of nickel with pyridine are especially numerous[38,51–53].

When 1,10-phenanthroline is present in a Co^{2+} solution a small prewave has been observed[28,29,55,56], which is attributed to the adsorption of the complex $CoPh_n^{+}$, where $n = 2$ or 3.

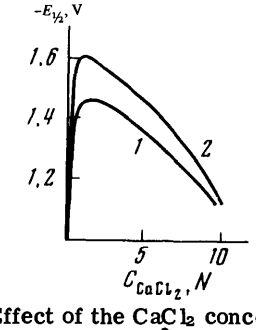


Figure 10. Effect of the $CaCl_2$ concentration on $E_{\frac{1}{2}}$ of the wave for the discharge of Fe^{2+} (1) and hydrogen ions (2); $[Fe^{2+}] = 2 \times 10^{-3}$ *N*, $[H^+] = 1 \times 10^{-3}$ *N*.[48]

7. STEPWISE NATURE OF THE REDUCTION OF COBALT, NICKEL, AND IRON

Two-electron waves are usually observed for the reduction of cobalt(II), nickel(II), and iron(II). However, Losev and Molodov[19] have shown that the transfer of the second electron is not simultaneous with the transfer of

the first, and under certain conditions the successive stepwise reduction of doubly- and multiply-charged cations can be observed.

In the presence of 1,10-phenanthroline two reduction waves are obtained[40-42,55,56] in solutions of Co^{2+} salts, these correspond to the successive transfer of a single electron in each stage. It has been suggested that under these conditions not only a Co^0 complex but also a Co^+ complex is stabilised. The waves have been shown to be irreversible and the limiting current of the first wave is diffusional in nature[40,56].

Single-electron waves were also observed in the investigation of complexes of iron with 2,2'-bipyridyl (Bipy) in an acetonitrile solution with rotating platinum and dropping mercury electrodes in tetraethylammonium perchlorate supporting electrolytes. Three waves are observed, which correspond to the reduction: to Fe^+ ($E_{\frac{1}{2}}^{I} = -1.45$ V) and then to Fe^0 ($E_{\frac{1}{2}}^{II} = -1.70$ V; s.c.e.); as Tanaka and Sato have shown[54], the third wave ($E_{\frac{1}{2}}^{III} = -2.0$ V) corresponds to the reduction of an uncharged complex with the formation of $[Fe(Bipy)_2]^-$.

The formation of a rather stable complex with a metal in a zerovalent state during the reduction of iron-group metals has been advanced repeatedly as a more or less substantiated hypothesis (see, for example, Refs. 25 and 57). The existence of such a complex has been proved[58] unambiguously with the aid of radiopolarography, in the investigation of the cyano-complexes of nickel labelled with ^{63}Ni. As has been shown[58], the ordinary polarogram and radiopolarogram of a solution of 1×10^{-3} M $NiCl_2$ in 0.1 M KCl are almost identical (Fig. 11). However, when 2.5×10^{-3} KCN is added to the solution, instead of a single wave on the ordinary polarogram three waves are observed, whereas on the radiopolarogram there is only one wave with $E_{\frac{1}{2}}$, which almost coincides with the $E_{\frac{1}{2}}$ of the main (second in order) wave. An increase in the concentration of KCN in the solution led to a decrease in the diffusion current of the first wave and to a decrease in the corresponding amount of radioactive nickel in the mercury drop. A further increase in the KCN concentration (to 10^{-2} M) leads to the disappearance of the first and second waves; on the polarogram there is only one wave with $E_{\frac{1}{2}} \simeq -1.5$ V, and the radioactive nickel is completely absent from the mercury drop (Fig. 12). On this basis it was concluded[58] that a stable complex with Ni^0 is formed (at sufficiently high KCN concentrations).

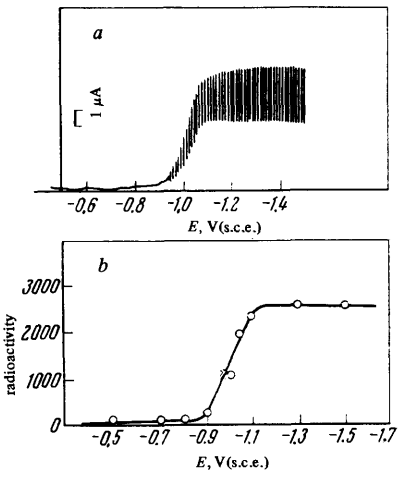


Figure 11. Comparison of the classical polarograms of nickel (a) and radiopolarograms (b); nickel chloride concentration 1×10^{-3} M, supporting electrolyte 0.1 M KCl.[58]

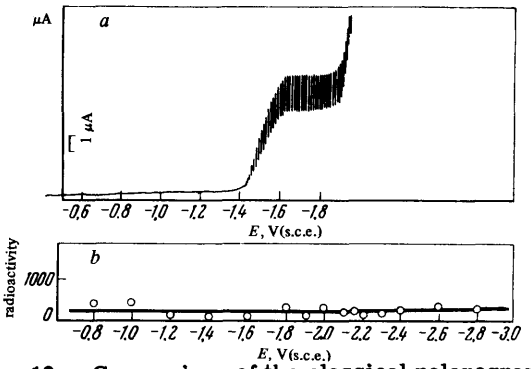


Figure 12. Comparison of the classical polarograms of nickel (a) and of radiopolarograms (b); nickel chloride concentration 1×10^{-3} M, supporting electrolyte 0.1 M KCl + 1×10^{-2} M KCN.[58]

8. FORMATION OF WAVES WHICH ARE CATALYTIC IN NATURE

Catalytic waves which are observed in the polarography of solutions containing cobalt and nickel salts with addition of sulphur-containing amino-acids have been considered sufficiently fully in Mairanovskii's review[59] and also in his monograph[60]. These publications systematised almost the entire literature up to 1965. Consequently, we will only briefly consider the catalytic waves of cobalt in the presence of organic additives. During the period that has elapsed since these two publications there have been no significant changes in opinions on the mechanism of the formation of catalytic hydrogen waves produced by certain organic compounds in the presence of cobalt salts; the mechanism for the production of such waves is still not fully explained.

Brdička[61] was the first to describe (in 1933) the unusual waves observable in the polarography of solutions which contain a cobalt salt and certain compounds with a mercapto-group. Since the wave for the reduction of Co^{2+} precedes the catalytic wave for the release of hydrogen, Brdička[62] and other investigators (see, for example, Ref. 63) have proposed that catalytically active centres form metallic cobalt, which is released at the surface of the mercury drop. To verify this point of view, Brdička[64] made a preliminary electrolysis of a solution at a stationary mercury cathode at a potential at which Co^{2+} is discharged but there is still no catalytic release of hydrogen. In the opinion of Brdička, under these conditions metallic cobalt will accumulate on the surface of the mercury drop. The catalytic wave should rise sharply if the metallic cobalt participates in this reaction. If the preliminary electrolysis were to have no effect on the height and form of the catalytic wave it would indicate that the metallic cobalt is not formed at the surface of the mercury drop. In Brdička's experiments the preliminary electrolysis did not alter the characteristics of the catalytic wave. This work has a definite effect on the formulation of ideas about the mechanism of the catalytic wave formed by certain organic molecules in the presence of cobalt and nickel ions. Most

investigators assume that a complex of the cobalt ion with the organic molecule acts as a catalyst.

Substances which contain a mercapto-group are known [60] to show catalytic activity in the absence of Co^{2+} or Ni^{2+} ions from the solution, but in the presence of the latter the catalytic activity of thiols increases sharply. The increase in the catalytic activity of thiols in their formation of complexes with Co^{2+} is linked, according to Mairanovskii [60], with the increase of the charge of the catalyst by two units, which from the point of view of the influence of the electrical double layer should facilitate the transfer of an electron to these species.

The greatest catalytic activity in the presence of Co^{2+} and Ni^{2+} is exhibited by compounds which simultaneously contain amino- and mercapto-groups. The catalytic effect observable in solutions of such compounds is determined by the action of all the active groups in the molecule. Using the example of the waves produced by cysteine and its derivatives, in which either amino-groups (*NN*-diacetylcysteine) or carboxyl groups (diethyl ester of cysteine) are blocked, Sunahara [65] has shown that blocking of the amino-groups leads to the complete loss of the catalytic activity of the cysteine whereas esterification of the carboxyls has hardly any effect on the characteristics of the catalytic wave. Mairanovskii therefore suggested that in catalysts containing both amino- and mercapto-groups the catalytic activity is due mainly to the amino-groups, whereas the adsorbability of the catalyst is determined mainly by the mercapto-groups. From this point of view, Mairanovskii [66] explains the observed parallelism between the ability of the catalysts to suppress the polarographic maximum, that is, their adsorbability and the height of the catalytic wave they produce. The adsorbability of the catalysts, which under strictly equal conditions determines the limiting catalytic currents is increased (in general) as the size of the catalyst molecule or the number of mercapto-groups in the molecule is increased. As Mairanovskii noted [60], this circumstance is evidently explained by Ito's observation [67] of the approximately proportionate increase in catalytic activity with increase in the number of cysteine residues in the composition of the protein-catalysts.

The height of the catalytic wave increases with the catalyst concentration and the curve for the dependence of the height of the wave on the concentration of the catalytically active substance is reminiscent of a Langmuir adsorption isotherm [60].

The influence of the pH on the catalytic waves due to complexes of cobalt or nickel with thiols is extremely complex. Maximal height of the waves is observed at some definite pH of the solution, as was noted by Březina and Gultjaj [68].

The catalytic activity of cobalt and nickel is usually regarded as an example of complexes with thiols; however, it is known that cobalt and nickel also increase the catalytic activity of pyridine [69], moreover the catalytic activity of pyridine is appreciably higher in the presence of Co^{2+} than in that of Ni^{2+} at the same concentration. It is especially high when both cobalt and nickel are present together in the solution. The catalytic wave which appears in the polarography of solutions of a complex of cobalt or nickel with pyridine has a surface nature. This is shown, for example, by the temperature dependence: as the temperature is raised the height of the catalytic wave falls rapidly and at a temperature above 35°C (in a solution with 0.1 *N* pyridine, 0.1 *N* pyridinium chloride, and 5×10^{-4} M cobalt and nickel salts) the wave is no longer observed [69].

Several new examples of organic compounds (including some which do not contain sulphur) which give catalytic waves in the presence of cobalt or nickel in the solution have recently been observed, e.g. 1,2-pyridylazoresorcinol dimethylglyoxime [70]. In this instance the height of the wave is several orders of magnitude greater than the diffusion current according to the metal ion. This allowed Vinogradova and coworkers [70] to use the catalytic wave of the complex with dimethylglyoxime for the analytical determination of nickel and cobalt in the negligibly small concentration of 2×10^{-8} M.

In certain instances in the presence of organic catalysts nickel gives catalytic waves or prewaves not connected with the release of hydrogen. For example, Tur'yan and coworkers [51,71-74] investigated in detail the nature of the similar catalytic waves observable in the polarography of thiocyanato-, pyridine, and thiourea complexes of nickel. The polarographic catalytic prewaves of nickel in the presence of various organic compounds, which although they contain sulphur in their molecule belong to several different classes of organic compounds, have been investigated [75]. In this study [75] the influence of additions of thioacetamide (Ta), thiourea (Tu), ethylthiourea (TuEt), diethylthiourea ($TuEt_2$), phenylthiourea (TuPh), thiosemicarbazide (Ts), rubeanic acid (dithiooxamide, DTO), unithiol (Ut), and thiocyanate (SCN^-) on the polarographic behaviour of Ni^{2+} (1 M $NaClO_4$; pH 6.25) was investigated. In every instance two catalytic prewaves were observed in the range $E = -0.6$ to -1.0 V (s.c.e.), not connected with the catalytic release of hydrogen. The following sequence of catalytic activity of the sulphur-containing compounds was observed: $Tu \simeq Ta < TuEt < TuEt_2 < TuPh < SCN^- < Ut < Ts < DTK$, which with the exception of SCN^- (Ut and DTO were not investigated in this plan) correlate with the adsorbability of these compounds at the mercury electrode. It was suggested that the catalytic prewaves investigated were due to chemical retardation in the stage of formation of polarographically active complexes, evidently with participation of the adsorbed ligand in most instances.

Calusaru [76] found that Co^{2+} forms a complex with nitrohydroxylamine (in an ammoniacal buffer solution). This leads to some decrease in the Co^{2+} wave and to the appearance of a catalytic wave of hydrogen with a characteristic maximum (in ammoniacal solution and in veronal acetate buffer solutions, starting from pH 6.12). Its height is maximal at pH 8.35 and is independent of the ionic strength of the solution. Nickel also forms a complex with nitrohydroxylamine but this leads only to splitting of the nickel wave [77].

It has been suggested [76,77] that catalytic waves are formed in the reduction of complexes of cobalt with substances which exhibit at least two chelate-forming functional groups. One of them is adsorbed on the mercury and the other shows a donor–acceptor function in relation to hydrogen ions.

Mark and Reilley [78] reported that in the presence of many amines which do not contain sulphur in their molecules Ni^{2+} gives a catalytic wave which appears at more positive potentials than the wave for the discharge of $[Ni(H_2O)_6]^{2+}$. Having studied in detail the mechanism of the electrode process with participation of *o*-phenylenediamine, Mark [79] concluded that the catalytic wave is due to the reduction of a complex formed on the surface of the electrode.

Hence catalytic waves of the most varied nature are formed in solutions of Co^{2+} and Ni^{2+} not only in the presence of thioamino-acids but also in the presence of various

classes of organic and inorganic compounds. The conclusion that the presence of groups which contain sulphur is a necessary condition for the appearance of a catalytic effect[80] is incorrect in the light of recent results.

It must be stated that Brdečka's work[64], in which he carried out a preliminary electrolysis, cannot serve as proof that metallic cobalt does not participate in the formation of a catalytic wave. The fact is that when a solution is electrolysed at a mercury surface the nature of the release of the iron-group metals is more complex than appears at first glance.

Two versions of the formation of a metallic phase in the discharge of ions on mercury can be proposed. In the first, the discharge of the ions is accompanied by the diffusion of metal atoms or their aggregates into the bulk of the mercury, where the cobalt or iron subsequently crystallise, or intermetallic compounds are formed, as happens for nickel.

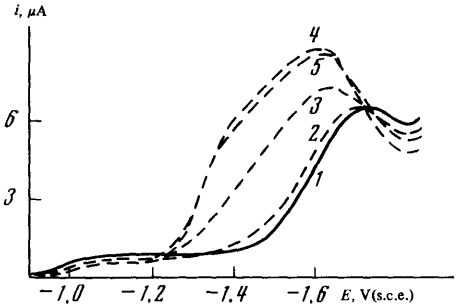


Figure 13. Polarograms of 4×10^{-4} M $CoCl_2$ + 2.3×10^{-4} M cysteine in a borate buffer (pH 9.2) in the presence of various amounts of surface-active substance—poly(vinyl acetate), 10^{-3}%: 1) 0; 2) 1; 3) 2; 4) 3; 5) 4.8.[57]

In the second, the formation of the metallic phase takes place on the surface of the mercury drop. This can be facilitated by the presence of adsorbed layers on the surface of the mercury drop. Owing to the local increase in current density on the mercury, crystallites of the metal will be produced (including nickel; nickel intermetallic compounds are subsequently produced as a result of the reaction of nickel crystals with the mercury).

The existence of a metallic phase on the mercury drop is also a complex phenomenon. The crystallites of the metallic phase are known to "sink" in mercury[81]. It is natural to assume that this process should depend upon the charge at the surface, the nature of the adsorbed layers, and other factors which influence the surface tension of the mercury. At a certain moment of time the nuclei break away from the surface and diffuse inside the mercury drop. Therefore there are no grounds for expecting the accumulation of the solid phase on a suspended mercury drop, as Brdečka[60] did. Under the conditions of his experiment a stationary process was established and the concentration of the metallic phase on the mercury remained constant (it did not depend on the period of electrolysis).

Evidently, when the solution contains a substance which is strongly adsorbed on the mercury it can inhibit the mixing of the solid (cobalt) and liquid (mercury) phases. When at the surface of the mercury there is a solid phase of a metal at which the hydrogen overpotential is considerably less (as happens, for example, for cobalt) than on mercury, then one may expect the discharge of hydrogen ions to be facilitated.

What has been stated above is supported by the fact that the catalytic effect for cobalt is appreciably greater than that for nickel. Cobalt has just as low a solubility in mercury as has nickel, but unlike nickel it does not form intermetallic compounds with mercury[82-85]. Nickel does not exhibit the ability to form compounds with mercury, which hinders the release of nickel on the mercury as an individual phase[82-85].

The recent work of Kolthoff and Mader[57] is extremely interesting in this connection. They recorded a cobalt wave for an insignificant concentration of it in the solution (4×10^{-4} M) in the presence of a little cysteine (2×10^{-4} M), that is, when the catalytic wave of hydrogen is absent from the polarogram. Then a surface-active substance which does not exhibit catalytic properties—poly(vinyl acetate) (PVA)—was added to the cell and a catalytic wave appeared and increased in height (as the PVA concentration was increased) (Fig. 13).

The addition of PVA to a solution which gives catalytic waves when polarographed increases the height of the catalytic wave and shifts this wave to less negative potentials (Fig. 13). However, these investigators start from the determinative role of a complex with zerovalent cobalt. They think[57] that the complex is stabilised in the presence of PVA.

It is noteworthy that iron behaves like cobalt in relation to mercury and consequently if the reason for the appearance of hydrogen waves is the formation of a phase which reduces the hydrogen overpotential, then in the presence of iron salts waves of this type should also be observed.

Ivanov and Ioffe observed this type of wave[48] on polarographing a solution of an Fe^{2+} salt in the presence of a surface active tetrabutylammonium (TBA) cation under conditions when the adsorption of this cation is greatly increased—in concentrated salt solutions (10 *N* $CaCl_2$). A sharp maximum is formed, the height of which is about 50 times that of the limiting diffusion current for iron (Fig. 14, curves *4* and *5*).

On the photomicrographs of a hanging mercury drop obtained[48] at the potential of the peak copious evolution of hydrogen is evident. At a potential more negative than that of the peak the liberation of hydrogen gradually ceases. It must be emphasised that the descending branch of the maximum is in the range of the negative peak of TBA adsorption.

We have also observed waves which are reminiscent in properties of the catalytic waves of hydrogen in solutions of cobalt and iron on the addition of a solution of sodium hypophosphite (curve *3* in Fig. 15); in the absence of these metals sodium hypophosphite is polarographically inactive[86]. The introduction of hypophosphite leads to the formation of the alloy Co_xP_y, insoluble in mercury, playing the part of a new solid phase on the mercury and it was noted earlier[87] that on an alloy of Co and P of a certain composition the overpotential of hydrogen liberation is lower than on cobalt. In every instance a film is formed on the mercury surface and has such a high surface activity that when hypophosphite is introduced into the solution the period of oscillation of the capillary is increased about tenfold, which leads to a change in the form of the wave and an increase in the limiting current (cf. Fig. 15, curves *4* and *5*). The formation of a similar wave for nickel is observed only at high concentrations of

hypophosphite but then the wave mentioned is insufficiently sharp: it almost merges with the background.

In support of the formation of a solid phase on mercury in the discharge of the ions of the Group VIII metals there is the recent work of Astley and Harrison [88]. By combining the method of superimposition of a triangular-wave potential with the impedance method they showed that on an electrode in the form of a hanging mercury drop the cobalt released from a 1×10^{-2} *N* $Co(NO_3)_2$ solution in the presence of KSCN (1–4 M) is formed either as an amalgam or as a phase surface layer of solid cobalt; in the latter instance the process is limited by the rate of nucleation and growth of the cobalt crystals.

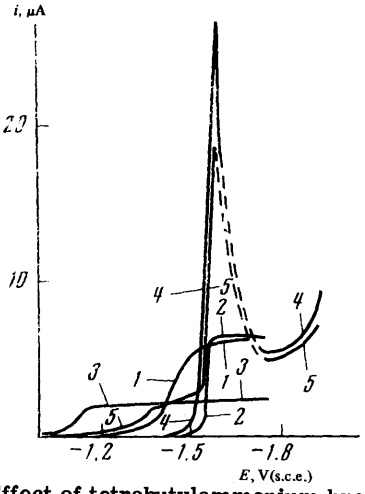


Figure 14. Effect of tetrabutylammonium bromide (TBA) on the kinetics of reduction of Fe^{2+} ions: 1) 1.0 *N* KCl, pH 5.5; 2) 1.0 *N* KCl, 1×10^{-3} *N* TBA; 3) 10.0 *N* $CaCl_2$, pH 5; 4) 10 *N* $CaCl_2$, 0.3×10^{-3} *N* TBA; 5) 10 *N* $CaCl_2$, 0.3×10^{-3} *N* TBA, pH ≃ 3. In every instance $[Fe^{2+}]$ is 2×10^{-3} *N*.[48]

The waves for the release of hydrogen, which resemble in properties the catalytic waves which are also observed in the polarography of solutions of metals of the platinum subgroup [49,89,90], and the heights of these waves are to the first approximation inversely proportional to the solubility of the metal in mercury or its ability to form intermetallic compounds with the mercury. For example, palladium, which is capable of forming intermetallic compounds with mercury, does not give such waves, despite the fact that the overpotential of hydrogen on palladium is appreciably less than that on mercury. The waves for the release of hydrogen in the presence of rhodium chloride [8], which have properties reminiscent of those of catalytic waves, were also observed on the addition of hypophosphite and certain aldehydes and ketones.

Hence it can be assumed that in at least several instances the waves are of a catalytic nature, observable in the presence of metals of Group VIII, due to the depression of the overpotential for the discharge of hydrogen on Group VIII metals, formed on mercury as a result of the discharge of the metallic phase. This conclusion does not contradict Gul'tyai and Mairanovskii's conclusion [91] that Co^{2+} accelerates only those catalytic processes which proceed either on the surface of an electrode with participation of an adsorbed catalyst or in a very thin layer adjacent to the electrode.

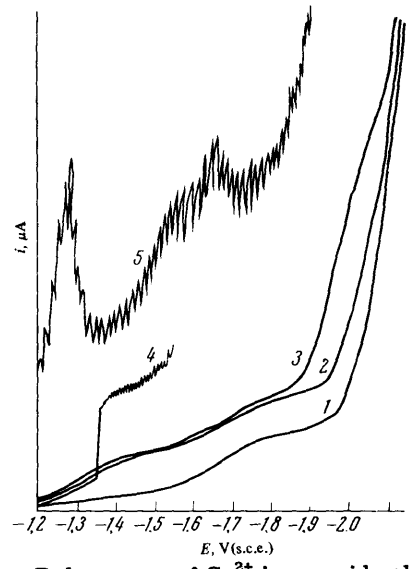


Figure 15. Polarogram of Co^{2+} in an acid solution (pH 2.97) on the addition of sodium hypophosphite. Curves: 1) supporting electrolyte 0.1 *N* KCl + HCl; 2) ditto + Co^{2+} (0.64×10^{-3} M); 3) as for 2 but + 1×10^{-2} M HPP; 4) and 5) as for 3, but the capillary drop period was arbitrarily increased and consequently also the wave height. [8]

There are also results [92,93] on the formation of catalytic hydrogen waves in the presence of chromium(III) (with bipyridyl) so that this property is intrinsic not only for Group VIII metals, but also for all metals, the hydrogen liberation overpotential (or that of other reactions with the participation of a proton) on the surface of which is lower than on mercury. In this instance the presence in the solution of PVA, which forms some similar "grids" which hinder the penetration of the microcrystal inside the mercury drop, is necessary for the appearance of a catalytic current. The magnitude of the effect should depend on the stability of this grid, in addition to other factors.

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The ions of our metals lie in the following order of the increase in the negative values of the half-wave potentials: Ni, Co, Fe.

In dilute aqueous solutions, most often used as a saline supporting electrolyte (alkali metal halides and perchlorates), each ion gives one two-electron wave; the $E_{\frac{1}{2}}$ for these ions lie in a rather narrow region of potentials, from −1.1 to −1.4 V (s.c.e.). Under these conditions the electrochemical process is irreversible. The nickel, cobalt, and iron ions exist in the solution as the hexahydrates.

An increase in the concentration of an indifferent electrolyte usually has a marked effect on the half-wave potential and limiting currents; this influence is mainly symbathic for all the three cations considered. In studying the influence of an indifferent electrolyte, it is essential to take into account the following effects which frequently act simultaneously:

1. A decrease in the negative values of the ψ_1-potentials as the concentration of the cation of the indifferent electrolyte is increased leads to a shift in the $E_{\frac{1}{2}}$ of the wave of our ions to more negative potentials; this effect is appreciably noticeable when the cations of the indifferent electrolyte have a charge of +2 or more, as, for example, in using calcium chloride. The limiting currents in concentrated solutions of the supporting electrolyte are lower than in dilute solutions.

2. The adsorption of ions of an indifferent electrolyte, of a foreign ligand, or of a complex formed by the metal ion concerned. As regards the specific adsorption of the ions of an indifferent electrolyte, in the instances we have considered it is usually necessary to take into account the specific adsorption of only the anions on the electrode surface, which occurs despite the negative charge of the electrode surface. This phenomenon is usually encountered in using rather concentrated solutions of halide ions and the specific adsorption increases very markedly in the order F^-, Cl^-, Br^-, I^-. This effect leads to an increase in the negative values of the ψ_1-potential, which in turn causes a shift in $E_{\frac{1}{2}}$ along the potential axis to more positive values.

A shift in $E_{\frac{1}{2}}$ also results from the reconstruction of the hydrate sheath of the ion, the introduction into the inner coordination sphere of a foreign ligand, such as the halide ions, OH^-, CN^-, CNS^-, and also a series of organic and inorganic ligands (those negatively charged and those without a charge), which are capable of forming a rather stable complex with the cation. The introduction of a foreign ligand into the hydrate sheath is facilitated by dehydration, which leads to a decrease in the negative values of the half-wave potential and an increase in the reversibility of the electrochemical process. Usually on the polarogram there appears a second wave at potentials more positive than the $E_{\frac{1}{2}}$ of the wave for the discharge of the completely hydrated ion.

On reaching a certain concentration of the complex-forming substance (the organic ligand or the anion of the supporting electrolyte) the complex formed is more stable than the hexahydrate. This leads to a shift in $E_{\frac{1}{2}}$ in the negative direction along the potential axis and frequently to a decrease in the limiting currents of the corresponding waves.

The influence of the above effects is mainly analogous for all three of the metals being considered. The influence of the composition of the supporting electrolyte is maximal for Ni and gradually falls in the order Ni, Co, Fe, and the reduction of the nickel complexes in sufficiently concentrated chloride solutions takes place in the positive range of the electrocapillary curve. This can facilitate the discharge of the complex of composition $[NiX_4]^{2-}$, whereas reduction of the negatively charged complexes of cobalt and especially iron, which takes place on the negative branch of the electrocapillary curve will experience some retardation. The addition to the solution of a ligand which forms a stable complex with the metal ion can so increase the stability of the intermediate complex with a singly-charged ion that is formed that the two-electron wave is split into individual waves corresponding to the transfer of a single electron. Here there is observed a rise in stability and the complex with the metal is found in the zerovalent state.

The replacement of water by an organic solvent significantly affects $E_{\frac{1}{2}}$, the limiting currents, and the degree of reversibility of the waves for the discharge of iron-group metals. The organic solvent plays the part of a ligand and then its influence obeys the rules listed above. In addition, in the presence of an organic solvent there is a decrease in the adsorbability of the organic ligands or complexes with such ligands, which usually leads to an increase in the polarisation.

Under certain conditions (the presence of surface-active substances, optimal conditions of electrolysis) the release of Group VIII metals at the surface of a mercury drop leads to the formation of a new phase which adopts the role of an electrode with greatly different characteristics from a liquid mercury electrode. The formation of a solid phase leads to the appearance of new waves on the polarogram—catalytic waves for the discharge of hydrogen. The appearance of a new phase also affects the reversibility of the discharge of the metal ion.

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Chemistry Division,
All-Union Institute of
Scientific and Technical
Information (VINITI),
Academy of Sciences of
the USSR, Moscow

U.D.C. 541.63

Topological Ideas in Stereochemistry

V.I.Sokolov

In commemoration of the centenary of the birth of Lev Aleksandrovich Chugaev

An attempt is made to assemble data for various branches of organic and biological chemistry which can be related directly to the ideas of topology. Consideration is given to problems of topological isomerism and the topological chemical bond, as well as to routes for the synthesis of molecules similar in structure to various geometrical figures. Special attention is paid to catenanes, rotaxanes (hooplanes), and knots. Information is given on the occurrence of topological structures and mechanisms in Nature. A list of 117 references is included.

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1. INTRODUCTION

Stereochemistry examines the spatial relations between atoms and groups within a molecule and also between different molecules. The spatial relations of idealised entities (points, lines, figures) constitute the subject of geometry. Therefore stereochemistry, so long as it is not concerned with dynamic processes, i.e. static stereochemistry, can be regarded as the geometry of molecular entities. That branch of dynamic stereochemistry which is confined to examining processes involving only a change in the internal coordinates of the molecule, conformations—but not chemical reactions—corresponds to introducing the ideas of motion into geometry.

As stereochemistry developed, it became increasingly clear that the relative arrangement of entities was especially important, but, within certain quite wide limits, metrical data (bond lengths, angles) were of little significance. The requirements of configurational stereochemistry are substantially similar to those of topology. This suggests that topology is an adequate mathematical foundation for stereochemistry.

Certain aspects of chemical topology were first discussed in 1961 by Frisch and Wasserman [1]. In a broad sense attention was attracted to topology as a mathematical basis for stereochemistry by a series of articles and papers by the eminent Swiss chemist V. Prelog during 1967–1969 (see e.g. "Problems of Chemical Topology", a lecture given in Dublin on 3rd April 1968 [2]). We shall briefly examine the main stages in the development of stereochemistry from this point of view.

The first step was the formulation of a structural theory, going back to Butlerov (1891). Based on the concept of valency, it established that only n atoms of the total present in the molecule were in a special relationship with a given atom A, where n is the valency of A. Thus the establishment of a topological concept—bond order in general—constituted the essence of the first formulation of a structural theory. The actual arrangement of the atoms—bond lengths and valency angles—is still completely unspecified. In general, nothing prevents directly bound atoms from being further apart than unbound atoms. Only the property of connectedness with respect to A distinguishes these n atoms from the whole set. Hence in the first stage the concept of bonding between atoms is topological rather than chemical.

Let N points belonging to n classes be located in a space (or on a plane, as in the original draft of a structural theory). The valency of a point of the nth class is n, and the number of points of this class a_n, where

$$\sum_n a_n = N.$$

The points may be joined in pairs by a chemical bond without further restriction. This set of points will represent a molecule only if the valency of each point is n (possible variability of valency is ignored for simplicity). The necessary formal condition for the existence of a molecule is $\Sigma n a_n = 2k$, where k is an integer: i.e. the sum of the products should be an even number.

The discovery of optical activity and the isolation of optical isomers, both preceding the development of a structural theory, demanded explanations of the number of structural isomers, which this theory was initially unable to explain. The problem was solved with the emergence of configurational stereochemistry (1875). The geometry of the immediate environment of a given atom—the arrangement solely of the directly bound n atoms (for carbon $n = 4$)—was specified in the tetrahedral model. In this well known history the difference between the van't

Hoff and Le Bel models is interesting for the purposes of this Review. Significantly, it is immaterial for configurational stereochemistry whether the valence tetrahedron of carbon is regular (van't Hoff) or irregular (Le Bel). Strictly speaking, the tetrahedron is always irregular if the substituents are different. A typical feature of stereochemistry—the neglect of metrical relations—is clearly apparent here. The valence angles of the tetrahedron can vary within very wide, though fully determinable, limits without change in configuration. A limit is reached when a coplanar arrangement of the substituents is achieved, when the system becomes achiral†. It is noteworthy that disregard of the metrical aspect of relations between entities is characteristic of topology.

It is appropriate here to define the most important stereochemical concept, configuration. In the Reviewer's opinion an adequate definition is lacking, at least in Russian-language textbooks. The following formulation may be suggested: *the configuration of a fragment is the short-range arrangement of the atoms, which is invariant with respect to the operation of rotation about single bonds*. The absence of superfluous detail enables systems possessing central and other types of chirality to be covered by this formulation.

The van't Hoff–Le Bel tetrahedral model played a decisive part in the practical development of stereochemistry, although the detailed geometry was in some sense a retrograde step in comparison with Pasteur's general ideas on molecular asymmetry as the cause of optical activity.

A direct development of the van't Hoff–Le Bel approach was Werner's coordination theory, which was based on the octahedron ($n = 6$). The success of this theory, which brought harmony into the previously chaotic world of complex compounds, was the first evidence of the universality of stereochemistry, rapidly extending beyond the limits of organic chemistry. When experimental workers came to study compounds of elements in higher periods, they encountered structures in which coordination numbers other than 4 and 6 were realised.

A trend became established to synthesise new molecules corresponding to well known geometrical figures. The progress made in this direction will be examined in Section 2. Subsequent Sections will be concerned with molecular entities for which the concept of topological isomerism is significant, together with their real analogues (catenanes–rotaxanes, isomers of clathrate type connected with the concepts of "inside" and "outside", etc.).

The examination of topological structures is not only intrinsically of great cognitive interest, in the sense of the opportunities for realising mathematical entities in a material, molecular form (where will the limits be reached?). It is no less significant that the actual properties of molecular systems may cause behaviour which is topologically indeterminate but nevertheless almost the same as for a topologically ideal system. This appreciably broadens the range of application of topological ideas and concepts. The clearest example is provided by rotaxanes (see later). While being a combination of cyclic and acyclic molecules mutually arrange in a definite fashion, they behave in effect as catenanes, since the very great steric hindrance makes destruction of this combination impossible without breaking a chemical bond. A less strict analogy to the "atom in cage" topological type is found in clathrates, in particular the subtype of compounds which could be termed "conformational clathrates". Each Section will consider both ideal topological entities and their real analogues.

Several important questions are completely ignored in the Review–the formal concept of Möbius cyclic π-electron systems first formulated by Heilbronner [7] and developed by Zimmerman [8,9] especially in relation to organic photochemistry, topological aspects of aromaticity [10], the systematic formalisation of stereochemistry in terms of topology developed in a series of papers on "Chemistry and Logical Structures" by Ugi et al. [11] on the basis of the concepts of Bourbaki's French school of mathematics.

2. REALISATION IN CHEMICAL MATERIAL OF RIGID THREE-DIMENSIONAL STRUCTURES NOT REQUIRING THE CONCEPT OF TOPOLOGICAL ISOMERISM

During recent years several authors [12–16] have discussed the problem of the polyhedra corresponding to various coordination numbers and the rearrangements of ligands occurring in such systems ("polytopic rearrangements"). A fundamental mathematical condition here is Euler's theorem—the first theorem of topology—according to which $V + F = E + 2$, where V, F, and E are the numbers respectively of vertices, faces, and edges.

There exist five regular convex polyhedra—tetrahedron, cube, octahedron, dodecahedron, and icosahedron—whose faces are respectively triangles, rectangles (squares), triangles, regular pentagons, and triangles. With the exception of the dodecahedron, they are all represented in molecular structures. Unsubstituted cubane was synthesised in 1964, [17] and its chemistry has since been developed considerably. Published data on simple derivatives of tetrahedrane are contradictory [18–20]. However, the existence of the tetrahedral ligand P_4 has been proved in complexes of platinum-group metals [21]. Several types of octahedral molecules are known, besides complexes of metals having coordination number 6, corresponding to a centred octahedron. The purely carbon octahedrane, which would have represented a C_6 molecule, is merely a fragment of the diamond lattice. Nevertheless, the octahedral molecule $C_2B_4H_6$ is known [22]. Carboranes-12, having the form of an icosahedron, have been widely studied‡.

In 1964 Woodward et al. [24] synthesised the unsaturated hydrocarbon triquinacene $C_{10}H_{10}$, which forms, as it were, half a dodecahedral molecule



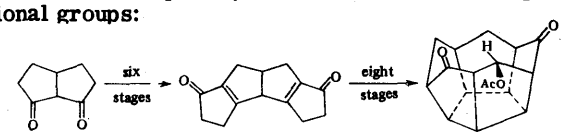
and may be a convenient precursor thereof. The same paper [24] reported the intention of subsequently studying the behaviour of triquinacene as an olefinic ligand in metal complexes, but further communications have not followed. However, such complex formation would have opened up prospects for dimerisation and also for obtaining compounds of "caged atom" type.

A different route for synthesising dodecahedrane, from two subunits—C_5 cyclopentane and a C_{15} fragment termed "peristylane"—has been chosen by Eaton and Mueller [25].

†Estimation of the energy required to convert tetrahedral into planar carbon shows that it exceeds the dissociation energy of the carbon–carbon bond [3]. The possibility of achieving a planar configuration of carbon has been examined by Hoffmann et al. [4,5], who have also discussed the possible stabilisation of a trigonal pyramid [6]

‡A review has appeared [23] on polyhedral organic molecules.

Starting from *cis*-bicyclo[3,3,0]octane-2,8-dione, they obtained the chosen peristylane derivative containing three functional groups:



(the structural similarity between peristylanes and [5]circulenes is obvious—see later). No information was given on the further plan of synthesis. High thermal stability was predicted[12] for dodecahedrane, with a stable carbanion consequent on effective delocalisation of the charge over the surface.

The requirement that the quadrivalency of carbon should be maintained probably makes the existence of a purely carbon icosahedron impossible. According to Euler's theorem this figure has 20 faces and 30 edges, with 5 edges meeting at each vertex, which implies that every atom is directly bound to at least 5 neighbours. Because of the variation in the type of bond this geometry becomes possible for carboranes $C_2B_{10}H_{12}$, in which all the atoms, including the carbon atoms, are formally six-coordinate. One valence is directed towards a group situated outside the ring system. However, $MC_2B_9H_{11}$ systems have been obtained in which the metal atom is unsubstituted[26,27]; derivatives of lower carboranes with an unsubstituted carbon atom have also been prepared[28]. The diversity of carborane structures is probably far from exhausted. The possibility of realising rigid non-convex polyhedra is of great interest from the point of view of structural topology. There are certainly no formal prohibitions of their existence with a sufficiently large number of vertices, and the availability of experimental methods for partly breaking down the structure of polyhedra (e.g. by removing one boron atom) may pave the way to the preparation of rigid non-convex polyhedra.

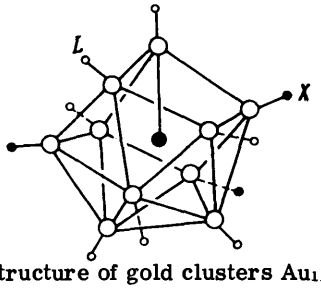
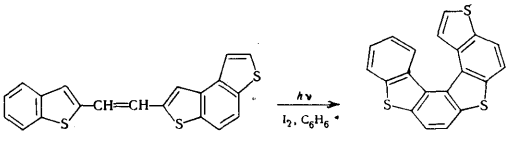


Figure 1. Structure of gold clusters $Au_{11}L_7X_3$ (where L = triphenylphosphine, and X is an anionic group).

Clusters form a special group of organometallic compounds, whose chemistry has been developed only during the past decade[29]. These molecules contain closed systems of metal atoms (usually of a single metal). At first only planar clusters were known, but now three-dimensional clusters have also been obtained, whose structure has been established by X-ray examination. Gold clusters have been studied fairly thoroughly, e.g. $Au_{11}L_7X_3$,[30-32] which has been interpreted as a centred icosahedron in which the site of three vertices is occupied by a single atom (Fig. 1). Another example of a metal cluster will be considered later in connection with "atom in cage" isomerism. Although ideas on the nature of the bond between the metal atoms in clusters are still fairly vague, there is no doubt about the existence of this bond, covering the whole cluster system, as is indicated in particular by the close similarity of all distances between metal atoms, including the internal atoms.

A clear example of the realisation of three-dimensional geometrical models is provided by the helicenes—molecules having the form of a fragment of an infinite screw surface—the first and for a long time the only representative of which, hexahelicene, was prepared and resolved into optical enantiomers by the brilliant work of Newman and his coworkers[33-35]. A characteristic property of this molecule—optical activity due to the presence of an actually asymmetric chromophore, which reflects the chirality of the screw surface—immediately attracted the attention both of theoreticians and of experimentalists. However, the investigations were complicated by the difficult accessibility of the compounds. Theoretical calculations of the absolute configuration of hexahelicene by different methods[36-41] gave discordant results.

More rapid progress has been made with heterohelicenes, mainly containing one or more thiophen rings, which have proved especially suitable for the necessary synthetic procedures. This route



has been developed in the laboratory of the Dutch chemist Wynberg[42-45]. In the course of this work the absolute configuration of a molecule of helicene type, [*d*]naphtho-[1,2-*d'*]benzo[1,2*b* : 4,3-*b'*]dithiophen, has been determined for the first time[44] from the anomalous dispersion. The same method has recently been used to establish the absolute configuration of 2-bromohexahelicene, which has been converted into hexahelicene[46,47]. With all three molecules the (−)-enantiomer forms a left-hand spiral, with absolute configuration M (Fig. 2). Thus the problem of hexahelicene, posed fifteen years ago, has been solved.

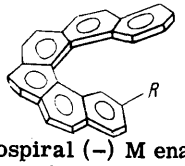
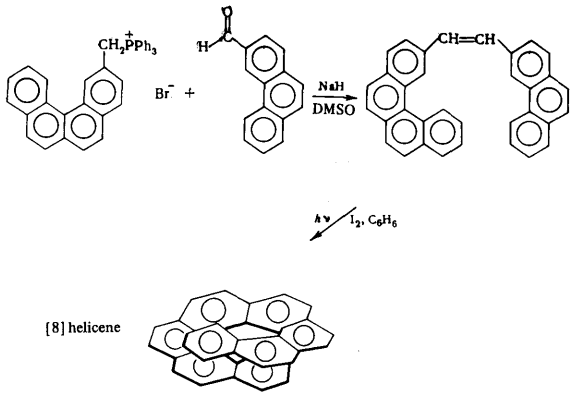


Figure 2. Laevospiral (−) M enantiomer of hexahelicene and 2-bromohexahelicene (R = H, Br).

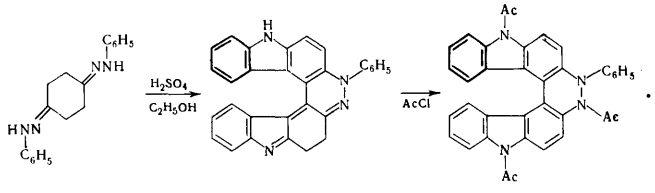
Martin et al.[48-50] have achieved considerable synthetic success in developing a new route to helicenes based on

the oxidative photocyclisation of 1,2-diarylethylenes:

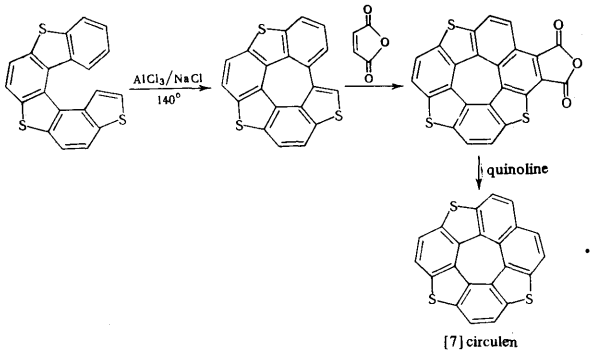


This method has already yielded homologous helicenes right up to [13]helicene, which consists of two turns of a screw surface.

It is interesting that the higher helicenes are spontaneously resolved into enantiomers on crystallisation. A good method for the optical resolution of helicenes is to crystallise them from an optically active solvent. Steric hindrance in these molecules is obviously so great that the packing together of molecules of different configurations in the same crystal becomes disadvantageous. Spontaneous resolution into enantiomers had previously been observed extremely rarely [51]. Azahelicenes have also been obtained in optically active form by a different method [52]:

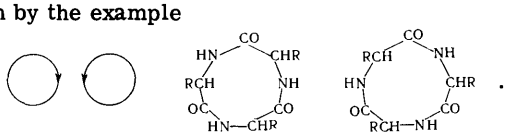


An interesting type of molecule is a circulene, a general name given by Dopper and Wynberg [53] to molecules comprising aromatic or similar rings fused on each side of a polygon. These workers examined cases in which the number of sides was n = 5–7. With a hexagon the planar aromatic molecule coronene, already known for quite a long time [54], is obtained. With n = 5 an example of a [5]circulene is corannulene [55]. The resulting stress forces the molecule out of a plane, making it buckle into a bowl shape. There is an obvious structural relation between [5]circulenes and peristylane, hetero-substituted derivatives of which can be obtained by further hydrogenation of hetero[5]circulenes. The first synthesis has been reported [53] of [7]circulenes, which should have a folded, corrugated form. In this case the perimeter of the molecule is longer than that of the planar coronene, whereas with corannulene the perimeter is shorter than in coronene. A [7]circulene has been obtained both by photocyclisation and from a [6]heterohelicene [53], which establishes a relation between two interesting classes of compounds:



3. TOPOLOGICAL ISOMERISM AND THE TOPOLOGICAL BOND

The widespread representation of molecules as geometrical figures, especially if all the atoms in the chain are identical, is generally used for carbon rings. However, the introduction of other structural entities (substituents, heteroatoms, etc.) leads to an internal orientation of the molecule, in which a definite direction of travel is distinguished. Such structural orientation assimilates a molecule to a path in the topological sense. The importance of structural orientation for stereochemistry is shown by the example



The two circles of the same radius are not congruent when displaced in a plane, if the direction of motion indicated by the arrow is taken into account: they are enantiomorphous if escape from the plane is forbidden. If the circles are replaced by cyclic molecules, an analogous orientation of the ring can be effected by means of different fixed sequences of non-equivalent groups. In *space* the above molecules (cyclotriglycines) can be superimposed as before. The situation is different, however, if the ring contains chiral centres differing in configuration. Combined with the fixed sense of the ring this leads to the appearance of a new type of isomerism, cyclostereoisomerism, which was actually discovered in cyclopeptides and their analogues [56, 57].

A most interesting branch of structural topology relates to information on the preparation and properties of molecules for which the concepts of topological isomerism and topological bonding are essential. Topology considers only those properties of a geometrical configuration which are preserved during deformations not involving rupture of lines and bonds§.

In general, two chemically non-bonded molecules can usually occupy independently any relative positions in space. However, a mutual arrangement is possible such

§Configurational stereochemistry presents more rigorous demands, since it takes into account the difference between enantiomers.

that it is not possible by any continuous transformation to achieve *all* relative positions: a chemical bond must be ruptured. In this case the combination of two species constitutes a new individual though composite molecule, whose integrity is accomplished by a new type of bonding, topological. This composite molecule is a topological isomer of the sum of the two separate component molecules [58]. According to Schill and Zürcher's definition [59] a characteristic feature of compounds having a topological bond is the property¶ that "main valency bonds must be broken in order to separate the complete molecule into its components, although no chemical bond is present between the two moieties".

We shall consider three types of topological isomerism. One depends on the relative arrangement of linear (one-dimensional) entities in space—whether looped or knotted—and is fundamentally impossible on a two-dimensional plane†. It includes catenanes, the first class of topologically bound molecules to be studied. They consist of at least two simple closed curves. Knotted lines are topologically isomeric with one simple closed curve, into which, however, they cannot be transformed without breaking the line.

The second type of topological isomerism is associated with the concepts of "inside" and "outside". It is realised even in a two-dimensional model, as is evident from the example



of topological isomerism in a plane. Chemistry is interested in the three-dimensional case of a "molecule in a cage". This type of topological isomerism, in contrast to catenanes, can be achieved only because atoms are real physical bodies, not geometrical points. The set of spheres formed by the van der Waals radii of chemically non-bonded atoms in a molecule effectively create a closed surface. As a consequence, an atom or a molecule in the inner region‡ is unable to pass into the outer region, since it is of finite size. From a purely chemical point of view a "molecule in a cage" represents an intramolecular analogy to inclusion compounds—clathrates.

Whereas in the first type of topological isomerism entities were represented by two lines, and in the second type by at least one closed surface, open surfaces appear in the third type. It is fairly obvious that segments of cylindrical surfaces can be joined on the catenane principle: this is a trivial analogue of the linear case. It is more interesting that they can be twisted any number of times n. Thus a cylinder ($n = 0$) is topologically isomeric with a Möbius strip ($n = 1$) and with all higher figures having $n > 1$. The upper limit of n is imposed by the width of the strip and the diameter of the cylinder.

¶This definition, which was given for catenanes, is valid for other classes, and also in some measure for analogues, of compounds having a topological bond, e.g. rotaxanes (see later).

†For non-self-intersecting figures.

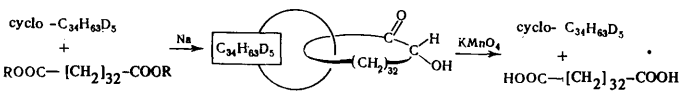
‡It is implied that the enclosing molecule forms a two-sided closed surface, to which Jordan's three-dimensional theorem applies.

4. CATENANES, ROTAXANES, AND KNOTS

Ideas on the synthesis of such molecules, which consist of two entwined rings, i.e. mechanically rather than chemically bound compounds, like links in a chain—hence the name *catenanes*—have been expressed more than once by different scientists, beginning at the latest with Willstätter [1]§. However, experimental work on this problem began only little more than a decade ago. In view of the availability of a review [59] and a monograph [61], of which the latter has been translated into Russian, it appeared advisable to present a somewhat abridged account of the problem of catenanes.

In order that steric hindrance by non-bonded atoms should enable one ring to pass through another, both rings should be large, each containing more than twenty atoms. A prerequisite for such investigations, therefore, was the development of methods for the synthesis of macrocyclic compounds, which was largely accomplished by the 1950s.

Two principles—statistical and directed—are now known for the synthesis of catenanes. In 1960 Wasserman [58, 62] obtained the first reliable evidence for the formation of a catenane, by subjecting the diester $ROOC.[CH_2]_{32}.COOR$ to acyloin condensation in the presence of the partly deuterated cyclic hydrocarbon $C_{34}H_{68}$:



In a random synthesis the probability that a linear molecule will undergo cyclisation at the same time as it has passed through a macrocyclic ring is extremely small. The yield of catenane in this method of synthesis is therefore negligible, and its formation was proved by isotopic labelling and mass spectrometry.

Further work on statistical synthesis used the metathesis of alkenes on catalysts including compounds of transition metals [63]. Wasserman, Ben-Efraim, and Wolovsky [64, 65], using intermediate cycloalkenes and a catalyst comprising tungsten hexachloride, ethylaluminium dichloride, and ethanol, obtained a mixture of cyclic oligomers up to at least C_{120}. Metathesis on transition metals is an intermolecular reaction. With a sufficiently large ring, however, this may be followed by intramolecular reactions. Some of them may yield catenanes, knots ("nectinodanes"), and Möbius strips ("plectanes"), as can be seen from Scheme 1. [65]

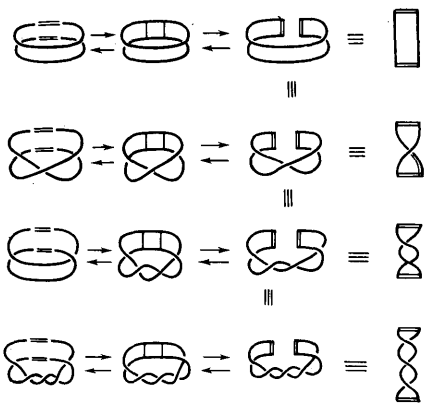
Although a circle can be deformed continuously into the edge of a Möbius strip, the statistical probability of achieving such a conformation is very small. It is another matter if some favourable factor is operating, e.g. coordination of double bonds of the cyclic molecule with a metal. In 1970 Wolovsky [65] and Wasserman et al. [66] published simultaneously very similar results on the metathesis of *cis*-cyclododecene on a tungsten catalyst, which indicated the formation of catenanes. The xylene-soluble fraction of the product was subjected to continuous mass-spectrometric analysis¶ while the temperature was gradually raised. A monotonic increase in the mass

§An interesting essay on these questions appears in Kostyanovskii's booklet [60], directed at the non-specialist reader; some historical information will also be found.

¶Kostyanovskii [67] in 1965 mentioned mass spectrometry as a convenient method for detecting catenanes.

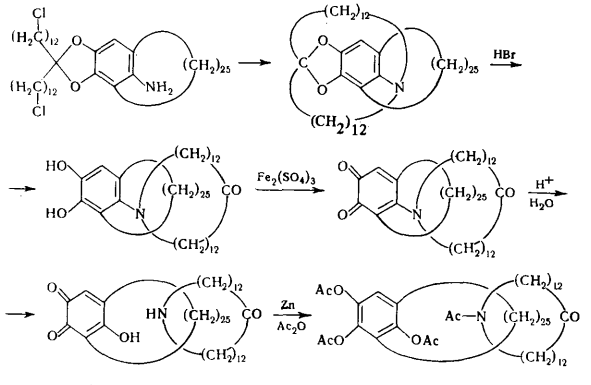
number of the most intense peak was found. At a certain temperature, however, peaks corresponding to lighter masses also showed a sharp increase in intensity. This phenomenon was explained by thermal rupture of the catenanes, the most abundant of which probably comprised C_{72} and C_{84} single rings. If the reason had been irregular cracking of monocyclic hydrocarbons, the mass spectrum would have shown an increase in intensity of a whole group of ions of closely similar mass. These workers adduced other arguments in support of the formation of catenanes (including multicatenanes), which will not be discussed here. It depends on the probability that a macrocyclic ring will buckle in a certain way, and this distinguishes it from Wasserman's first synthesis [58], which was governed by the probability that a chain would pass through a ring. Other aspects of the statistical synthesis of catenanes have been discussed [68, 69].

Scheme 1



A fundamentally different route was used in the directed synthesis of individual catenanes. Work on this problem began in the laboratory of Lüttringhaus during the 1950s as a development of the synthesis of "ansa" compounds. For a long time the desired result could not be obtained [70]. Success was finally achieved by Schill [71, 72], who synthesised the first [2]catenane by the sequence of reactions in Scheme 2. This synthesis made use of

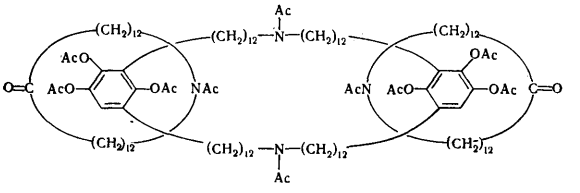
Scheme 2



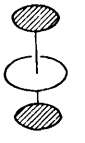
special supports or "scaffolding", by means of which the required groups were retained in a fixed position. They were then selectively removed by procedures which did not affect the remainder of the molecule. As a result it was possible to achieve the synthesis of two interlinked macrocyclic rings joined by a bridge, which was eliminated in later stages.

The "scaffolding" method requires great selectivity and great experimental skill. It ensures correct assignment of structure and provides an approach to the synthesis of higher catenanes. The first [3]catenane was obtained by Schill and Zürcher [73] (Scheme 3). The actual working out of a route for a directed synthesis is an extremely difficult task. In practice Schill's group have used the same chemical reactions in all their syntheses of catenanes and rotaxanes.

Scheme3



Wasserman [58] had previously and with complete justification defined a catenane as a topological isomer of two uncombined cyclic molecules. The molecular nature of the entities, however, leads to the curious situation that, if a linear molecule with bulky groups at its ends (dumbbell-shaped) passes through a macrocyclic ring, the resulting system



behaves analogously to a catenane: its components also cannot be separated without rupture of a chemical bond. Such systems are termed *rotaxanes*†.

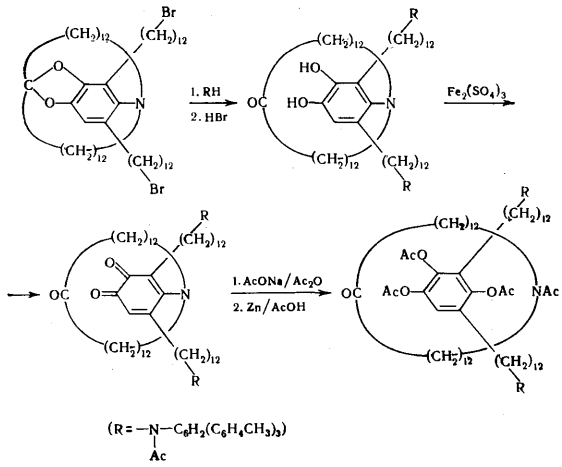
Schill and Zollenkopf's synthesis [74] is shown in Scheme 4. Nevertheless, in contrast to catenanes, rotaxanes are topologically indistinguishable from the simple sum of linear and cyclic molecules. This is shown especially clearly by work on the statistical synthesis of rotaxanes [75, 76]. A macrocyclic C_{30} acyloin was bonded to a polymeric carrier—Merrifield's resin—and subjected to repeated treatments with decane-1,10-diol and triphenylmethyl chloride in a solvent containing pyridine. Mild alkaline hydrolysis was followed by the chromatographic isolation of 6% of a rotaxane, in which either the ring or the linear portion could be broken selectively. Harrison [76] has recently detected extraordinary selectivity with respect to the size of the ring. Simply heating the macrocyclic hydrocarbon with 1,10-bistriphenylmethoxydecane in solution to 120°C leads to *equilibrium* between the rotaxane and the separate components *only for* C_{29}.

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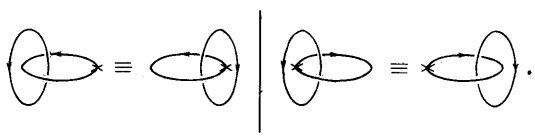
†Inclusion compounds with cyclodextrins are directly relation to rotaxanes (see later).

In the presence of trichloroacetic acid the reversible removal of one triphenylmethyl group makes it possible to obtain rotaxanes with C_{25}–C_{29}. With a larger ring the triphenylmethyl group will obviously pass through freely. The remarkable simplicity of this synthesis of rotaxanes should stimulate further investigations on these lines.

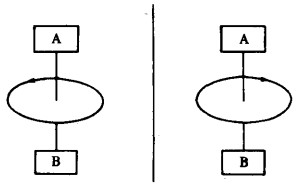
Scheme 4



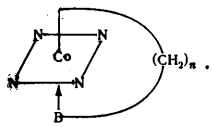
All catenanes and rotaxanes known hitherto have contained at least one ring of symmetrical structure, so that problems of chirality were not directly involved in these systems. If, however, this ring were oriented by unsymmetrically arranged heteroatoms or groups (indicated by an arrow in Scheme 5), the possibility of enantiomerism would arise, as is shown by the rotaxane in Scheme 5. A [2]catenane will likewise be enantiomeric if its two rings are not identical and are oriented:



Scheme 5

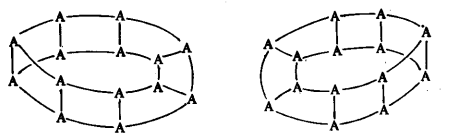


Coordination compounds of metals can be used as "scaffolding" for building up catenoid structures. A system consisting of a metal atom fixed in a planar quadridentate ligand, with the two remaining positions in the coordination octahedron joined by a long chain, would be analogous to a catenane. The best simple example of such a complex, the approach to whose synthesis is self-evident, is an amminepolymethylenecobalt derivative of the type



The macrocycle is completed at the cobalt atom by means of a σ-bond with carbon and a donor-acceptor bond with a basic group B (e.g. phosphine or amine). This structure is formally of the catenane type, but differs in having nitrogen–cobalt coordinate bonds between the two rings.

Catenanes are the only class of topological molecular structures that have yet been synthesised. It would be an extremely interesting problem to construct a molecule having the geometry of a one-sided surface—the Möbius strip

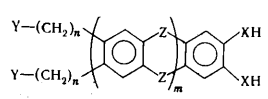


Double cyclisation of a long molecule in the form of a fairly stiff band can be effected two ways—XY, X′Y′ to give a cylinder, and XY′, X′Y a Möbius strip



(cf. scheme of metathesis of cycloalkenes). In this statistical method of synthesis the probability of each mode of cyclisation would be close to 0.5 (in contrast to catenanes).

A suitable model molecule, which can easily undergo conformational flexing, can be constructed by introducing for instance aromatic fragments. Thus the A–A units can conveniently be benzene rings joined by short bridges comprising one or two atoms. These compounds are evidently oligomers (in particular oligoarylates) in size and structural form. For example, the edge of the cylinder for the molecule



will contain $N = 4m + n + 4 = 4(m + 1) + n$ atoms, and the edge of the Möbius strip twice this number. If we assume that $N = 20$, which seems quite reasonable, we have

$m = 1;\ 2;\ 3;\ 4.$
$n = 12;\ 8;\ 4;\ 0.$

It must be borne in mind, however, that the overall rigidity of the system increases with increase in m, owing to the accumulation of aromatic rings, and N should increase. The connecting bridges could be either oxygen atoms or methylene groups.

Another aspect of the problem of the Möbius strip concerns the occurrence of conformational transitions of macrocyclic compounds in solution, not the construction of a rigid molecule. This applies to the case in which the A–A units are interlinked not covalently but by weaker interactions, e.g. of donor–acceptor type. With a suitable arrangement of heteroatoms and functional groups a large ring (having $N \simeq 40$ or more) may assume the conformation of the edge of a Möbius strip.

Finally, it must be noted that the Möbius strip should exist as two enantiomeric forms, and therefore possess inherent optical activity, as a consequence of its property of orientability, even when constructed of identical atoms.

It has been shown above that, as in the metathesis of cycloalkenes, not only catenanes but also knotted molecules ("nectinodanes") and twisted molecules ("plectanes") can be obtained [65,78]. These possibilities follow directly from solving the geometrical problem of cutting a cyclic strip which has been twisted n times. Such molecules have not yet been synthesised. In an early paper Wasserman [62] estimated the minimum number of atoms from which the simplest knot, a trefoil, can be formed as $n \geqslant 50$. The first search for a knotted molecule was then undertaken in the random cyclisation of a C_{66} diester.

A remarkable property of knots is their chirality. Because it has been twisted in a definite direction, a knotted molecule should possess intrinsic optical activity. The optical rotation of the trefoil knot $[CH_2]m$ has been calculated [78] on Kirkwood's theory. With $m = 66$, when interactions of non-bonded atoms produce no appreciable distortions in the structure, the calculation gives $[\alpha]_D = +2.1°$, i.e. $[M]_D = +19.4°$, for the absolute configuration depicted on the left-hand side of



The smallness of the absolute rotation introduces uncertainty into the assignment of configuration, since even slight departures from the ideal structure employed in the calculation may produce a change in sign. Optical activity may be an indication of the formation of knotted molecules in random synthesis [62].

No attempt at directed synthesis has been reported. Scheme 6 suggests a synthesis for a trefoil knot using an octahedral metal complex as matrix.

5. TOPOLOGICAL ISOMERISM CONNECTED WITH THE CONCEPT OF "INSIDE" AND "OUTSIDE"

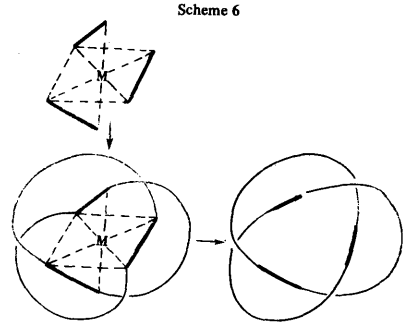
No single example is yet known of purely topological isomerism due to the enclosure of one molecule (or atom) in the space bounded by another molecule, without specific interactions between them. We shall therefore consider here more or less close analogies arising in real systems.

Inclusion compounds or clathrates have long been known [79], in which molecules are located in the cavities of a crystal lattice formed by molecules having a different structure. Clathrates, whose structure was understood more than twenty years ago, are of no special topological interest, since the intermolecular bonds usually are easily broken when the crystalline state is disturbed.

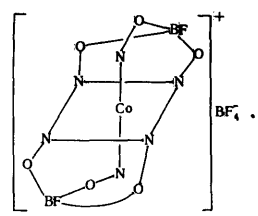
Cases are possible in complicated, conformationally mobile systems where some species may be "trapped" and retained by forces weaker than a covalent bond. An interesting example is the selective bonding of a xenon atom by myoglobin [80], which probably has a clathrate structure. Capture is accomplished in solution or in the crystal by the conformational mobility of the protein molecule. Hydrophobic interactions may play an important part here. Other examples provided by natural compounds will be discussed in the final Section of the Review.

Mention must be made of interesting systems in which isomerism of the "inside–outside" type is effected by a coordinate bond (encapsulation reactions). In 1967 Pedersen [81] discovered the class of cryptates, introducing into practice macrocyclic ligands containing several ethereal oxygen atoms ("crown ethers"). With suitable size and conformational mobility of the ring they form stable complexes with metal ions, mainly of Groups I and II, the selectivity depending on the structure of the ligand. Research on cryptates is developing rapidly [82–84], and analogous principles of complex formation have proved to be of biological importance (see later).

Scheme 6

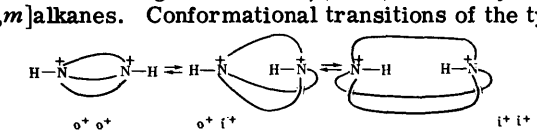


Boston and Rose [85] obtained a kind of clathratochelate containing a cobalt ion



The synthesis is based on the principle of treating an ordinary octahedral complex, having three bidentate ligands, with a reagent capable of "locking" the three ligands located on opposite faces of the octahedron.

In the same year 1968 Park and Simmons [86] studied the isomerism arising in salts of 1, $(k + 2)$-diazabicyclo-$[k,l,m]$alkanes. Conformational transitions of the type

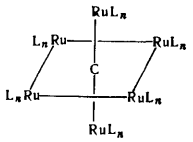


are possible in such macrobicyclic diamines when $k, l, m > > 6$‡. These equilibria have been studied in solutions of various acids by proton magnetic resonance. It is especially remarkable that encapsulation of halide ions occurs when $k = l = m \geqslant 9$. The corresponding isomeric salts, catapinates, are more sparingly soluble and are precipitated from solution. The [9,9,9]diamine will yield $i^+Cl^-i^+$[9,9,9]Cl^- only after standing at 25°C for five days, the reaction is more difficult with the bromide, and no catapinate is formed at all with the iodide, whereas the [10,10,10]diamine rapidly gives encapsulation products of Cl^-, Br^-, and I^-. Thus the steric requirements of the bicyclic molecule are fairly definite. It is very likely that the anion is retained in the "interior" by two hydrogen bonds.

‡Hydrogen or nitrogen directed outwards is denoted by o^+, and inside the molecule by i^+.

The inclusion compounds of graphite [87,88] form a peculiar class closely resembling clathrates. The occluded molecules are trapped in them by a single macromolecule, which does not in general enclose a portion of space. However, the actual conditions are such that escape of occluded molecules from the space between the layers is in practice difficult (e.g. high temperatures are required). During recent years analogous layer compounds (intercalation complexes) based on niobium and tantalum disulphides and diselenides have been discovered. The occluded molecules may be amines, e.g. pyridine or aniline [89,90]. Hardly any work has yet been done on these complexes, but they are attracting attention in connection with the problem of superconduction.

Several structures are known formally corresponding to the "atom in cage" type. They include the interesting organometallic carbide clusters [91]. The carbon atom situated at the centre of a regular octahedron formed by six ruthenium atoms



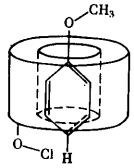
appears to correspond to the topological condition. However, the carbon–ruthenium distances are too small (1.88–2.12 Å), which undoubtedly indicates the presence of a chemical bond.

Organometallic chemistry is in general a suitable field of activity for seeking topological isomerism of the "inside–outside" type. Early attempts were made [92] to synthesise "cage" structures based on metallocenes. This is a practicable approach. An especially useful property of many organometallic compounds is their reducibility to the metal. If a compound is thus obtained in which the metal inside the cage is bound by a chemical bond (σ or π), a reducing attack on this bond can be conducted from outside the molecule, e.g. by electron transfer. However, it is not clear beforehand whether the resulting metal atom is sufficiently inert not to demolish the cage. In any case, the current state of the science allows such a problem to be investigated experimentally.

6. TOPOLOGICAL STRUCTURES AND MECHANISMS IN NATURE

An important factor for naturally occurring molecules, especially for macromolecules with their abundant possibilities of variation in conformation, is the relative arrangement, quite often a prerequisite for chemical interaction. Such systems are of direct interest in connection with the problems under discussion.

Natural complexes of clathrate type were the earliest to become known. Dextrin polysaccharides include cyclodextrins having cylindrical macromolecules. Molecules of a certain size are able to penetrate inside the cylinder [93], and their retention is assisted by hydrophobic interactions. The formation of such inclusion compounds with cyclodextrins or cycloamyloses has been used to resolve certain chiral molecules into enantiomers [94]. Breslow [95,96] has applied the formation of cyclodextrin clathrates to effect a kind of catalysis. If the linear portion of a molecule is placed inside the cylindrical macromolecule of a cyclodextrin, the groups outside (usually inert) are close to the agent and undergo uncharacteristic reactions. In this way it has proved possible to substitute chlorine in anisole solely in the *para*-position by the action of hypochlorous acid



and more rapidly than in the uncomplexed substrate. Breakdown of the clathrate gave a high yield of *p*-chloroanisole [95].

Preliminary clathrate formation has also enabled model esters to be hydrolysed with rate constants comparable with those found in the hydrolysis of esters by esterases [96]. The principle of preliminary favourable orientation of reactant molecules is adopted by enzymes. The high rates of enzymatic reactions are in fact known to be due to the formation of an enzyme—substrate complex, which can in some sense be regarded as a conformational but not a topological isomer of the separate enzyme macromolecule and substrate molecule§.

The great conformational mobility of biological macromolecules and the abundance of functional groups are closely connected with their biological functions. Thus it has been found quite recently [98,99] that the biological activity of peptide antibiotics of the valinomycin type involves the selective formation of simple complexes of cryptate type with alkali-metal ions, and ultimately the transport of these ions across cell membranes.

The formation in Nature's laboratories of extraordinarily complicated and highly specialised molecules suggests the probable occurrence of topological structures and mechanisms. Their identification, of course, involves very great difficulties. In fact, the disruption of the integrity of biological entities during study may change their structure beyond recognition. Nevertheless, clear evidence has now been obtained of the existence of catenoid deoxyribonucleic acids in the mitochondria of several cells, both pathogenic and normal. These first natural catenanes were discovered in 1967 by the American biochemist Vinograd and his coworkers [100,101], who obtained their electron micrographs. Individual macrocycles reached 5 μm. The micrographs clearly revealed also higher linearly linked catenanes up to a [7]catenane. Further work has shown that catenoid DNA are widely distributed.

Schill and Zürcher [59] have suggested a possible mechanism for the biogenesis of catenoid DNA on the basis of known properties of the Möbius strip. The hypothesis that cyclic DNA are constructed on this principle was first put forward some time ago by Wasserman [62]. Eight years later Burdick showed that it would not contradict the known properties of cyclic DNA [102]. If a Möbius strip twisted n time is cut along the midline, catenanes are formed whenever n is an even number; when n is unity, a single ring is obtained with a double circumference; and other odd values of n yield various knots [78]. The replication of double-strand Möbius DNA, which is equivalent to this slitting, thus naturally yields catenoid and knotted macromolecules (the latter have not yet been detected).

§During recent years experimental methods have been developed enabling a detailed study to be made of the character of the effective surface of macromolecules. It is advisable to term such work study of the topography of the surface of the molecule [97]: use of the term "topology" in these cases is incorrect.

In view of the probable existence in Nature of molecules simulated by one-sided surfaces like the Möbius strip, the existence of closed one-sided surfaces does not appear improbable. In three-dimensional space such surfaces can be realised only with self-intersection: i.e. the three-dimensional Jordan theorem is not applicable to them, and they do not divide space into internal and external regions.

The postulated possible existence of structures having such properties is directly related to the problem of membrane transport. The proposed topological hypothesis makes no demands on the size of the species to be transported (the migration of large molecules across membranes has recently become known[103]). The main idea is that, at least in some cases, no real penetration takes place *through* the membrane, which is a one-sided surface. We suppose that a particle Z is firmly attached to a site on the "outside" of the membrane (Fig. 3*a*). If a change in the conformation of the surface is now induced by this bonding or some other cause, the site may move "inside" (Fig. 3*b*), where the particle is removed from the membrane. Thus the apparent result is the penetration of Z through the membrane¶, which is actually a consequence of the conformational change in the surface—a special kind of allosteric effect.

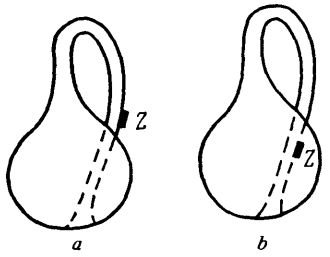


Figure 3. Illustration of the topological hypothesis of membrane transport.

The energy relations observed in membrane transport may be an indication of the energetics of this conformational change. Certain consequences can be deduced from the suggested model: (1) substances that change the permeability of membranes should exert an allosteric action and/or combine selectively with certain molecules or ions; (2) certain molecules known as good complexing agents will not, however, increase appreciably the permeability of membranes for the corresponding ions, owing to the absence of an allosteric effect; and (3) strong effectors will accelerate non-selectively the transport of various species owing to the enhanced conformational lability of the membrane. The specific chemical mechanisms of bonding both effectors and transportable species with the membranes can obviously be extremely varied. The separation of allosteric and complexing effects may assist a better understanding of the problem.

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¶Simple penetration of molecules through channels connecting "internal" and "external" regions may be prevented by the size of these channels.

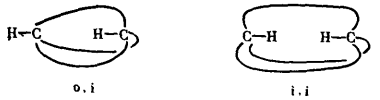
In the Reviewer's opinion structural topology is one of the growth points of modern stereochemistry. The technical difficulty of synthesising model compounds has hitherto been a strong restraining factor. The difficulties will probably diminish considerably during the next few years, after which rapid developments in this field must be expected, especially in the investigation of the chirality of topologically isomeric molecules. Without depending on the rate of experimental development, ideas arising from topology play an important part in the complex of concepts involved in modern stereochemistry.

ADDENDUM

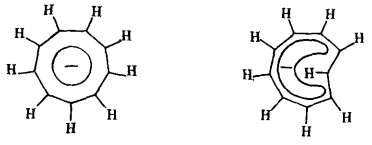
The ideas forming the subject of this Review have been further examined in several recent papers.

Schill et al.[104] have continued their directed synthesis of a catenane (Scheme 3), passing to a simpler compound by ozonolysis of the aromatic ring followed by reduction of the carbonyl groups to methylene. In this way they have obtained the ancestral [28, aza-25]catenane.

Park and Simmons[105] have extended their investigations of the conformational isomerism of macrobicyclic compounds, begun on diamines[86], to purely carbon systems. They have selectively synthesised i,i- and o,i-bicyclo-[8,8,8]hexacosanes



isomers whose structure is confirmed by the carbon-13 nuclear magnetic resonance spectra. Interconversion of the isomers has not yet been reported. A similar system, in which a hydrogen atom attached to a bridgehead carbon faces the interior of a rigid bicyclic molecule, has been prepared by Gassman and Thummel[106]. In this connection it is interesting that isomerism associated with the convexity or concavity of a planar polygon has already been observed[117] in the cyclononatetraenide anion



Research on cryptates is being vigorously pursued, both in the synthesis of new multidentate macrocyclic ligands and in their use for preparative purposes[107-111].

No weakening of interest is apparent in the preparation of polyhedra and other three-dimensional molecules, especially of the cluster type[112-115]. The trideca-atomic polyhedron of the carborane class is probably not convex[116].

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Institute of Organoelementary Compounds,
USSR Academy of Sciences, Moscow

U.D.C. 541.62

Ring-Chain Isomeric Conversions of Aldehydo-carboxylic and Keto-carboxylic Acids and Their Derivatives

R.E.Valter

Ring-chain isomeric (including tautomeric) conversions of aldehydo- and keto-carboxylic acids and their chlorides, amides, hydrazides, esters, and mixed anhydrides are reviewed. The possibilities of using physical methods (ultraviolet, infrared, and proton magnetic resonance spectroscopy) for the identification and quantitative determination of isomers are discussed. The effect of structural factors on the relative stability of isomers is analysed. Conditions are elicited under which interconversion occurs or equilibrium is observed. A list of 207 references is included.

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I. INTRODUCTION

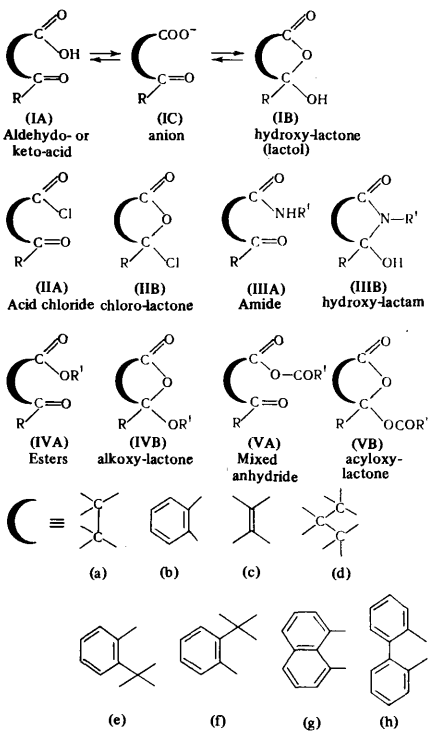
Ring-chain isomeric conversions are observed in organic molecules containing a multiple bond and a functional group capable of intramolecular addition at this bond. The structure of the molecule should enable the two groups to assume a relative arrangement suitable for the reversible intramolecular addition.

Ring-chain isomeric conversions are often termed ring-chain tautomerism [1]. Depending on the polarity of the bonds of the interacting functional groups, electronic and steric effects of substituents, and several other factors, however, three types of isomeric conversions may be observed. (1) In ring-chain tautomerism, equilibrium is rapidly established between open (A) and cyclic (B) forms in solution at room temperature. (2) In reversible ring-chain isomerism [2] both forms can be obtained separately, and are stable in neutral solvents at room temperature. The isomerisations A → B and B → A are effected by the action of acid or basic catalysts, by specific reagents, or on heating. (3) In irreversible ring-chain isomerism both forms are stable, but their interconversion can be achieved only in one direction (A → B or B → A).

Isomeric and tautomeric conversions must be clearly distinguished. Absence of tautomeric equilibrium can be reliably assessed, of course, only when both isomers have been isolated and it has been established that they are both stable in solution. If only one isomer has been isolated, e.g. A, and its stability in solution has been demonstrated, occurrence of the equilibrium A ⇌ B is still possible, displaced so far towards A that the concentration of the isomer B is below the limit of sensitivity of the method of identification used.

A previous review [1] did not differentiate between tautomeric and isomeric conversions. It had the defect of an uncritical approach to the results of early investigations, in which the structure of the isomers had been demonstrated only by chemical methods. The use of such methods to establish the structure of compounds capable of isomeric conversions is unreliable and a frequent source of error. As early as 1956 Hammond [3] wrote that, since spectroscopic methods had been developed after the period

Scheme 1



of the most active studies of ring-chain tautomeric conversions, there were grounds for expecting that in the near future a new stage would begin in the general investigation of these problems. Actually, quite a large number of investigations have been published during the last decade in which structures of open-chain and cyclic isomers and their interconversion have been examined by ultraviolet, infrared, and proton magnetic resonance spectroscopy.

The present Review summarises results only of those investigations, published mainly during the past decade,

in which the structure of the isomers was reliably established by spectroscopic methods. Attention has been paid mainly to—(i) spectroscopic characteristics enabling cyclic and open-chain forms to be identified and determined in mixtures, (ii) the relative stability of the isomers, i.e. the character of the equilibrium, (iii) the conditions under which isomeric interconversions occur, and (iv) the influence on the relative stability of the isomers exerted by the electronic and steric effects of substituents attached to the interacting functional groups and by the structure of the bridge connecting them. In order to analyse these questions in greater detail, we restrict our survey to aldehydo- and keto-carboxylic acids and their acid derivatives. Scheme 1 gives the general structures of the open-chain (A) and cyclic (B) forms examined (I)–(V) and the structures of the bridging units (a)–(h) joining the two functional groups. The structures (a)–(h) enable us to expect the existence of cyclic forms, but undoubtedly do not exhaust all possible cases.

II. ALDEHYDO- AND KETO-CARBOXYLIC ACIDS

γ-Aldehydo- and γ-Keto-carboxylic Acids (Ia–c)

Nucleophilic intramolecular addition of a carboxy-group to a carbonyl group is a rapid and reversible process[4], and the tautomeric equilibrium IA ⇌ IC ⇌ IB is established in solutions of γ-aldehydo- and γ-keto-acids. Independently of the structure of the molecule and of the substituent R, the carboxylate anion always has the open-chain structure (IC)[4–15]. Pascal[16] found that the equilibrium

$$\underset{\text{dimer of keto-acid}}{\text{IA...IA}} \rightleftharpoons \text{IA} \rightleftharpoons \text{IB} \rightleftharpoons \underset{\text{associated lactol (C=O...H–O)}}{\text{IB...IB}} \quad (A)$$

is established in solutions of methyl-substituted γ-oxovaleric acids in solvents of low polarity.

It was suggested[16] that the tautomeric equilibrium constant $K_T = a_B/a_A$ of aldehydo- and keto-carboxylic acids in solution should be determined using the equation

$$\lg(K_T + 1) = pK_a - pK'_a \quad (1)$$

where K_a is the acid ionisation constant of the carboxylic acid determined potentiometrically, and K'_a the true (theoretical) acid ionisation constant of the carboxylic acid A in the absence of the tautomeric equilibrium IA ⇌ IB. Use of the method[4,16–18] is restricted by the fact that it is extremely difficult to determine accurately the constant K'_a from the acidity constants of model acids of similar structure that are incapable of cyclisation. This has been done most accurately for *cis*-β-acylacrylic acids from the experimental acidity constants of the corresponding *trans*-acids[19]. Bell[4] determined the constant K'_a of *o*-formylbenzoic acid from a kinetic investigation of its catalytic action in the decomposition of nitramide and the mutarotation of glucose, whence he calculated the tautomeric equilibrium constant in aqueous solution (K_T = 14.8). This method is claimed to be more accurate.

Bowden[20,21] solved the opposite problem by substituting in Eqn. (1) values of K_T determined by proton magnetic resonance and the constants K_a determined potentiometrically: he calculated the true acid ionisation constants K'_a of several *o*-acylbenzoic and *cis*-β-aroylacrylic acids in 80% aqueous 2-methoxyethanolic solution.

The ketonic carbonyl band disappears from the infrared spectrum in the tautomeric conversion IA → IB of γ-keto-acids. Owing to the bending stress on the >C=O bonds in the five-membered ring of IB, the lactonic carbonyl bond is shifted to higher frequencies (1800–1770 cm^{-1}) than in the carboxy-group in the open-chain form IA (Table 1).

Table 1. Frequencies (cm^{-1}) of C=O bands in infrared spectra of γ-keto-acids in solution.

Formula (I)		Solvent	Form A		Form B, lactone	Ref.
	R		ketone, aldehyde	carboxyl		
CH_2	H	CCl_4	1749	1711	1795	22
	CH_3	CCl_4	1726	1758 (free) 1714 (bound)	—	16
CH_2	C_6H_5*	$CHCl_3$	1690	1710	—	23
	CCl_3	$CHCl_3$	1767	1724	1808	24
	H	dioxan	1699	1723	1778	20
	CH_3	dioxan	1706	1724	1776	20
	C_6H_5	dioxan	1681	1726	1781	20
	CCl_3	$CHCl_3$	1574 sh**	1721	1789	24
H	H	in KBr tablets	—	—	1795, 1761	25
	CH_3	dioxan	—	—	1763	19
H	C_6H_5	dioxan	1676	1713	1769	21
	CCl_3	$CHCl_3$	1786 sh	1715	1812	24

*β-Benzoyl-α-methylpropionic acid.
**sh = shoulder.

Determination of the tautomeric equilibrium constants of *o*-aroylbenzoic[26,27], *o*-acylbenzoic[20], and *cis*-β-aroylacrylic[21] acids from the infrared spectra is based on the postulated equality of the integrated intensities of the carbonyl bands in the spectra of esters of cyclic (IVB: νC=O = 1780 cm^{-1}) and open-chain (IVA: νCOOR = 1730 to 1720 and νC=O = 1700–1675 cm^{-1}) structure and the corresponding tautomeric forms (IA and IB) of keto-carboxylic acids. The reproducibility of the determination of the content of tautomeric forms is ±2–3%.[20,27] Satisfactory correlation is observed between the tautomeric equilibrium constants of *o*-*m*′(or *p*′)-X-benzoylbenzoic acids and the σ_m and σ_p constants of the substituents X respectively[26,27].

When proton magnetic resonance is used to analyse ring-chain tautomeric systems, it must be borne in mind that two cases are observed depending on the rate of the tautomeric conversion[28]: (i) with slow tautomeric conversions (on the p.m.r. time scale) the proton signals of the two forms are observed separately, and the tautomeric composition is determined from their relative intensities; (ii) with rapid conversions the proton signals of the two forms coalesce into a single signal, characterised by the mean chemical shift. Replacement of a less polar by a more polar solvent or additions of catalytic quantities of acids or bases may influence the rate of the tautomeric changes, and thereby change significantly the pattern of the p.m.r. spectrum[12,20,29].

The forms (IA) and (IB) are most often identified and determined by means of the signals from protons in the groups CH_3CO (IA) and $CH_3C(OH)O$ (IB: R = CH_3) (or in general AlkCO and AlkC(OH)O) for keto-carboxylic acids[13,16,17,20,29–32] and in the groups HCO (IA) and HC(OH)O (IB: R = H) for aldehydo-acids[9,11,12,14,15,18,22]. Signals of protons in other groups have been used more rarely[21,33]. In the p.m.r. spectrum of *o*-acetylbenzoic acid dissolved in hexadeuteriated dimethyl sulphoxide

Finkelstein[29] observed proton signals at 2.45 ppm† (CH_3CO) and 1.78 ppm ($CH_3C(OH)O$). The constant was determined from the signal intensities as $K_T = 2$. After catalytic quantities of hydrochloric acid had been added to the solution, the two signals coalesced into a single signal with a chemical shift of 2.02 ppm. In the p.m.r. spectra of keto-carboxylic acids, however, one common signal is most often observed, indicating the occurrence of rapid tautomeric conversions[16,17,20,31,32]. In the determination of the constant K_T it is assumed that the contents of the forms (IA) and (IB) in the tautomeric mixture are inversely proportional to the distances of their common signal from the corresponding signals in the spectra of fixed models, the esters (IVA) and (IVB)[20,31]. The constant K_T for β-formylpropionic acid[22] was determined from the intensity ratio of the signals of aldehydic and methine protons (9.54–9.66 and 5.66–5.83 ppm respectively).

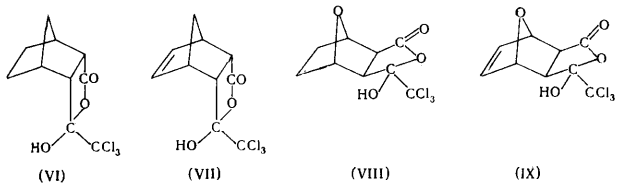
The disappearance of the chromophoric group (C=O) in the conversion of IA into IB is responsible for corresponding changes in the ultraviolet spectrum. However, absorption in the ultraviolet, governed by electron transitions in conjugated systems, cannot be interpreted as clearly as infrared absorption, where the presence of a particular multiple bond can be assessed unambiguously. The use of ultraviolet spectroscopy to determine the constants K_T in tautomeric systems of aldehydo- and keto-carboxylic acids is based on the postulate that the absorption by fixed models—the esters (IVA) and (IVB)—and the absorption by corresponding tautomeric forms of the acids (IA) and (IB) do not differ appreciably[22,31,34].

Little work has been done on the effect of the solvent on the tautomeric equilibrium. In more polar solvents the equilibrium is displaced towards the cyclic form[26,27,35]. However, contrary results have also been obtained[36]. The mechanism of the action of the solvent on the tautomeric system IA ⇌ IB is complicated. Intermolecular hydrogen bonds may play an important part in stabilising a particular form, the cyclic isomer showing a greater tendency to form such bonds involving both carbonyl and hydroxyl groups. Dilution of the solution[6,7,22], the use of pyridine or triethylamine as solvent, or their addition to existing solutions displaces the equilibrium towards the open-chain form[15,22]. In acid media the equilibrium is shifted in favour of the less acidic cyclic form[7]. No correlation could be found between the structure of *o*-acylbenzoic acids and the temperature dependence of the ring–chain tautomeric equilibrium[36,37].

Structural factors promoting intramolecular nucleophilic addition of the carboxyl to the carbonyl group can be divided into three types—(i) factors that enhance the electrophilic character of the aldehydic or ketonic carbon atom (the presence of electron-accepting substituents R, the absence of conjugation between the carbonyl group and an aromatic ring, etc.), (ii) factors that enhance the nucleophilic character of the oxygen atoms in the carboxy-group, and (iii) factors that bring carboxyl and carbonyl groups closer together in space, which is most favourable for intramolecular attack.

The carbonyl carbon atom becomes less electrophilic with the squence of substituents R = H, Alk, Ar. The equilibrium IA ⇌ IB is established in solutions of β-formylpropionic acid[22] and its chain-substituted derivatives[16,18,38]. The cyclic form is not detected in solutions of γ-oxovaleric acid[16]. The accumulation of two or three methyl groups in the chain brings about a steric approach of carboxyl and carbonyl groups (the *gem*-dimethyl effect[3,39]), and for ααβ-trimethyl-γ-oxovaleric acid[16] in 80% aqueous 2-methoxyethanol $K_T = 7.7$. Infrared spectroscopy provides evidence that β-aroylpropionic acids[23,40,41] and several of their more complicated analogues[42] have the open-chain structure in the crystalline state and in solution.

An increased tendency to form the cyclic modification has been observed[10,24] in a series of β-trichloroacetylcarboxylic acids. The −*I* effect of the trichloromethyl group is obviously operating here. The relatively high stability of the ring forms of the bicyclic keto-carboxylic acids



(VI) (VII) (VIII) (IX)

is due to the completely protected conformations of the *cis*-substituents (COOH and CCl_3CO) attached to the second and third carbon atoms of 1,4-*endo*-methylene- and 1,4-*endo*-oxo-cyclohexanes and -enes, which create the most favourable conditions for intramolecular nucleophilic attack.

Because of the steric approach of carboxyl and carbonyl groups, *o*-acylbenzoic acids (Ib), and especially *cis*-β-acylacrylic acids (Ic), show a greater tendency than do β-acylpropionic acids (Ia) to form the cyclic modifications. Three-dimensional models show that the open-chain forms of these acids (Ib–A and Ic–A) are able to exist only in the energetically disadvantageous non-coplanar form, which excludes conjugation of the π-bonds[43].

In solutions of *o*-formylbenzoic (Ib: R = H)[4,8,11,12,15,44,45] *o*-acylbenzoic (Ib: R = Alk),[5,20,29,31,32,35,45–50] and especially *cis*-β-acylacrylic (Ic: R = H, Alk)[17,19,25] acids the tautomeric equilibrium is displaced towards the cyclic form. The ketonic carbon atom in *o*-aroylbenzoic acids (Ib: R = Ar) is less strongly electrophilic owing to conjugation with both aromatic rings. In the absence of specific structural factors stabilising the ring form, *o*-aroylbenzoic acids have predominantly the open-chain structure in the crystalline state and in solution[20,27,31,34,45,51–56]. The tautomeric equilibrium constants of *o*-*m*'- or *o*-*p*'-X-benzoylbenzoic acids[26,27] in dioxan have values of 0.03–0.10, and those of *cis*-β-*p*-X-benzoyl-α(or β)-methylacrylic acids[21] lie in the range 1–26, the higher values being observed with acids having electron-accepting substituents X.

A methyl group in the 3- or 6-position of a 2-aroylbenzoic acid exerts a steric effect on the carboxyl and carbonyl groups, so that the equilibrium is shifted in favour of the ring form, with a 6-methyl group having the stronger effect. Methyl groups in the 2'- and 6'-positions of the aroyl substituent shield the carbonyl group sterically, and hinder cyclisation[34,52,57]. Predominance of the cyclic form has been noted in 2-benzoyl-3,4,5,6-tetrachlorobenzoic acid[27,31].

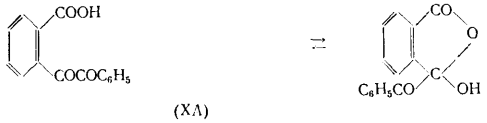
The series of 2-acetyl-6-X-benzoic acids shows[29] increase in the stability of the ring form with strengthening of the electron-donating power of the substituent X, i.e. with enhancement of the nucleophilic character of the oxygen atoms in the carboxy-group. Nitro-groups, independently of their position in the phthaloyl ring,

†Chemical shifts are always indicated on the δ-scale relative to TMS.

stabilise the open form [27,29,31,56]; the reason for this is not entirely clear.

Infrared spectroscopy has been used to investigate the structure of *o*-acylbenzoic acids in the crystalline state [31,45,58]. The isolation of one tautomeric form of an aldehydo- or keto-carboxylic acid in the crystalline state does not prove that this same form predominates in solution [3,31,35,49]. Interpretation of the infrared spectra is complicated by the presence in the lattice of stable intermolecular hydrogen bonds O–H...O=C (lactol), which split the carbonyl band of the lactol and shift it to lower frequencies than in solutions [31,42,45]. The spectra of concentrated solutions of keto-carboxylic acids in weakly polar solvents contain, besides the free carbonyl band of the lactol (1780–1770 cm^{-1}), also a band at 1750 cm^{-1} due to a bound carbonyl group [16,32,35]. The latter becomes less intense with dilution of the solutions, which distinguishes this band from absorption by monomeric carboxyl observed [16] in the same region. The main evidence of the ring structure (IB) in the spectra of crystalline compounds is the presence [6,31,58] of an intense, broad band due to a bound hydroxy-group (OH...O=C) at 3350–3150 cm^{-1}. In the spectra of crystalline keto-carboxylic acids (IA) the hydroxy-absorption of the dimeric carboxy-groups is apparent as a diffuse band at lower frequencies (3000 to 2600 cm^{-1}).

o-Formylbenzoic [44,45,58] and *o*-acetylbenzoic [29,31,32,45,58] acids have the ring structure in the crystalline state. Some *o*-acylbenzoic acids (Ib: R = Alk or more complicated substituent) have been obtained in the crystalline state as the cyclic modification [5,10,24,59], and others in the open form [35] or as a mixture with one form predominating [35,47–50,60]. Both isomers of benzil-*o*-carboxylic acid



(XA) (XB)

have been obtained in crystalline form [58,61], and the thermal isomerisation XB → XA has been accomplished.

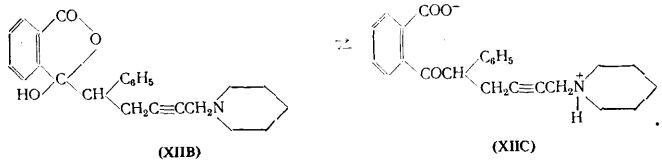
Three crystalline modifications of *o*-β-*N*-t-butylcarbamoyl-α-phenylpropionylbenzoic acid have been described which differ in their content of the tautomeric forms



(XIA) (XIB)

and in the involvement of the various carbonyl groups in the formation of intermolecular hydrogen bonds [50].

It is interesting that the acid (XII) can be isolated, depending on the conditions, as the lactol (XIIB) or the betaine (XIIC)[62]



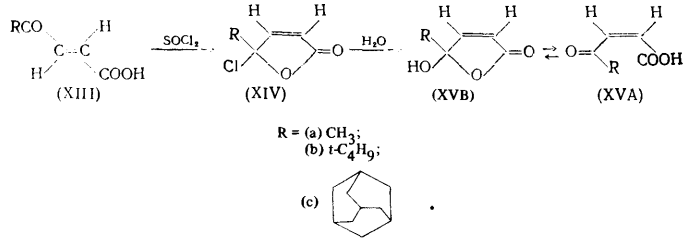
(XIIB) (XIIC)

The effect of the conditions of isolation on the isomeric composition of crystalline aldehydo- and keto-carboxylic acids has not yet been adequately studied. It is of interest to ascertain the effect of the temperature régime of crystallisation, the nature of the solvent, the temperature of the alkaline solution from which the acid is isolated by acidification, the pH of the medium after acidification, etc. These conditions probably play an important role, neglect of which makes nonsense of the search for rules relating the structure of the acids to their isomeric composition in the crystalline state.

cis-β-Formylacrylic acid [25,63,64], its αβ-substituted derivatives [9,15,65–68], and *cis*-β-acetylacrylic acids [13,17,69–71] in the crystalline state have the cyclic structure, which predominates even in solution. *cis*-β-Aroylacrylic acids have been isolated in the crystalline state either as the cyclic or as the open-chain isomer [6,7,72–75].

The geometrical isomerism of β-acylacrylic acids complicates the study of their ring–chain tautomerism. It is necessary to distinguish not only open-chain and cyclic forms but also *cis*- and *trans*-isomers of the form (IA). This problem is solved by proton magnetic resonance: the spin–spin interaction constant of the olefinic protons for αβ-unsubstituted *cis*-β-acylacrylic acids is 5.5–7 Hz, and that for the *trans*-isomers 16 Hz. [13,17,70,71] The *trans*-configuration has been identified [36,37] also from the infrared band due to out-of-plane deformation vibrations of the carbon–hydrogen bond at 980 cm^{-1}.

Scheffold [17] obtained the cyclic chloride, 5-chloro-2,5-dihydro-5-methylfuran-2-one (XIVa), by the action of thionyl chloride on *trans*-β-acetylacrylic acid (XIIIa):



(XIII) (XIV) (XVB) (XVA)

R = (a) CH_3; (b) $t\text{-}C_4H_9$; (c)

Careful hydrolysis of the chloride yields *cis*-β-acetylacrylic acid in the ring form (XVa–B). This compound is converted back to the thermodynamically more stable *trans*-isomer (XIIIa) on sublimation. Crystalline *cis*-β-acetylacrylic acid could not be obtained in the open-chain form (XVa–A).

Sugiyama [71] accomplished the isomerisation XIIIa → → XVa–B by exposing *trans*-β-acetylacrylic acid to a mercury lamp. An attempt to obtain the open-chain *cis*-isomer by the isomerisation of *trans*-β-pivaloylacrylic acid (XIIIb) was also unsuccessful. These experiments confirm the extraordinary stability of the cyclic forms of *cis*-β-acylacrylic acids.

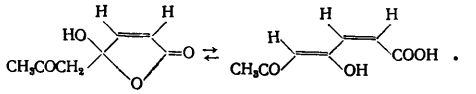
Kuchař [76] obtained a mixture of three isomers—(XIIIc), (XVc–A), and (XVc–B)—on acidifying an alkaline solution of 4-adamant-1'-yl-4-oxobut-2-enoic acid, but the evidence for the presence of the open-chain *cis*-form (XVc–A) was not entirely rigorous. Equilibria between cyclic and open forms were observed in acid and alkaline solutions of the 2- or 3-halogenated acids [33,37], but unfortunately the configurations of the open-chain isomers were not established.

Bowden [19] obtained unexpectedly high tautomeric equilibrium constants for *cis*-β-pivaloylacrylic acid (K_T = 94 ± 11) and *cis*-4-adamant-1'-yl-4-oxobut-2-enoic acid (70 ± 8) in 80% aqueous 2-methoxyethanol solution.

The introduction of methyl groups [6,7,17,19,21] and also of halogen atoms [33,77] as substituents attached to the olefinic carbon atoms in *cis*-β-acylacrylic acids stabilises the

cyclic form, a substituent having a greater effect in the β than in the α position.

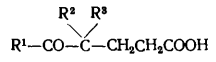
Simultaneous ring–chain and keto–enol tautomerism has been observed [78] in maleoylacetone:



(XVIB) (XVIA)

δ-Aldehydo- and δ-Keto-carboxylic Acids (Id–g)

Pentin [40,79–81] used infrared and ultraviolet spectroscopy to investigate the series of saturated δ-keto-carboxylic acids



(XVII)

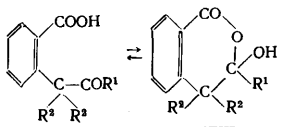
(R^1 = Alk, Ar; R^2 = H, Alk, Ar; R^3 = H, Br)

and found that they had the open-chain structure in the crystalline state, and when dissolved in chloroform and in carbon tetrachloride the cyclic form was not detected. The chain of three sp^3 carbon atoms evidently does not create sterically suitable conditions for the cylic form to be produced. Unfortunately, δ-keto-carboxylic acids having *gem*-dialkyl substituents on the chain carbon atoms were not examined, although they might be expected, by analogy with γ-keto-carboxylic acids [16], to form the cyclic isomers.

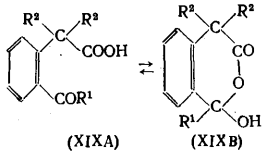
Table 2.

Compound	R^1	R^2	Structure in cryst.	Compound	R^1	R^2	Structure in cryst.
XVIII a	C_6H_5	H	A	XIX a	CH_3	H	A
XVIII b	CH_3	CH_3	B	XIX b	C_6H_5	H	A
XVIII c	C_6H_5	CH_3	B	XIX c	CH_3	CH_3	B
				XIX d	C_6H_5	CH_3	A

Infrared spectroscopy has been used to investigate the structure of crystalline *o*-acetonylbenzoic and *o*-phenacylbenzoic acids (XVIIIa–c in Table 2) and *o*-acylphenylacetic acids (XIXa–d) [82–85]



(XVIIIA) (XVIIIB)



(XIXA) (XIXB)

The state of equilibrium IA ⇌ IB was analysed [82,83] only from the results of chemical reactions. The acids (XVIIIb, c) and (XIXc), which contain a *gem*-dimethyl fragment, have the cyclic structure in the crystalline state. The acid (XIXd), in which the keto-group is conjugated with two aromatic rings, has the open structure, in spite of the presence of a *gem*-dimethyl fragment. Among the acids (XVIIIa–c) and (XIXa–d) only *o*-αα-dimethylacetonylbenzoic acid (XVIIIb) reacts with diazomethane to form a cyclic ester, 3-methoxy-3,4,4-trimethylisochroman-1-one. In solutions of the acid (XVIIIb) the equilibrium is supposed [83] to be displaced completely in favour of the cyclic form, owing to the absence of conjugation between the keto-group and the aromatic ring.

Spectroscopic [30] and indirect chemical [57,86,87] evidence indicates that tautomeric equilibrium is established in the 8-acylnaphthoic acids (Ig) and is absent from *o'*-acylbiphenyl-*o*-carboxylic acids, which have the open structure (Ih–A). Data on the possible formation of cyclic isomers by completion of a seven-membered ring are contradictory [88,89].

III. ACID CHLORIDES

Chlorides of γ-Aldehydo- and γ-Keto-carboxylic Acids (IIa–c)

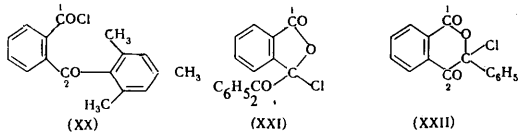
Formation of the cyclic modification of chlorides of keto-carboxylic acids is favoured by factors making the carbon atom of the COCl group more strongly electrophilic and the oxygen atom of the keto-group more strongly nucleophilic. Because the former is so strongly electrophilic, owing to the $-I$ effect of the chlorine atom, chlorides of β-acylpropionic [22,90–94], *o*-acylbenzoic [45,51,55,56,95–101], and *cis*-β-acylacrylic [6,7,17,25,75,76] acids have exclusively the cyclic chloro-lactone structure (IIB) in the crystalline state and in solution.

The infrared spectra of γ-chloro-lactones (IIa–c–B) are characterised by an intense lactonic carbonyl band at 1820–1805 cm^{-1} (IIa–B), 1810–1790 cm^{-1} (IIb–B), and 1800–1760 cm^{-1} (IIc–B, the band sometimes being split [17]) and the absence of absorption by the ketonic or aldehydic carbonyl in the range 1725–1660 cm^{-1}. The state of aggregation of the compound has little effect on the carbonyl frequency of γ-chloro-lactones.

γ-Chloro-lactones form two series of derivatives with nucleophilic reagents [6,98,102]. Since it has been demonstrated spectroscopically that the tautomeric equilibrium IIA ⇌ IIB is not present in solutions, the formation of two series of derivatives can be explained by the presence of two electrophilic centres—the carbon atoms of the C=O and C–Cl groups—in the chloro-lactone molecule. Stronger nucleophiles polarise the carbonyl group and attack its carbon atom preferentially; weaker nucleophiles attack the carbon of the C–Cl group. Reactions with primary amines, for example, yield *N*-monosubstituted amides (IIIA or IIIB) in the former case; in the latter case amino-lactones are obtained, for which in solution the tautomeric equilibrium amino-lactone ⇌ imino-acid is established [6,102].

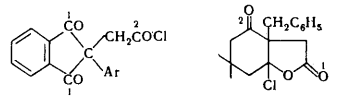
o-2′,4′,6′-Trimethylbenzoylbenzoyl chloride has the open structure (XX) owing to steric shielding of the keto-group [55,57,96], and is almost the sole exception [57] in the series of *o*-acylbenzoyl chlorides. It has recently been established [101] that, contrary to early investigations [61], both chlorides of benzil-*o*-carboxylic acid have cyclic

structures, 3-benzoyl-3-chlorophthalide (XXI) and 3-chloro-1,4-dioxo-3-phenylisochroman (XXII).



(XX) (XXI) (XXII)

1) $\nu_{C=O}$ 1797, 1733‡ 1) $\nu_{C=O}$ 1808 (4,6) 1) $\nu_{C=O}$ 1764 (3,6)
2) $\nu_{C=O}$ 1673 2) $\nu_{C=O}$ 1694 (1,2) 2) $\nu_{C=O}$ 1726 (1,7)



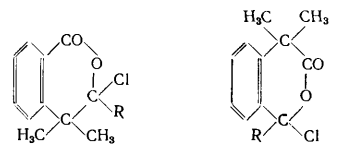
(XXIII) (XXIV)

1) $\nu_{C=O}$ 1740, 1700 1) $\nu_{C=O}$ 1818 (4,0)
2) $\nu_{C=O}$ 1800-1770 2) $\nu_{C=O}$ 1720 (1,7)

2-Aryl-1,3-dioxoindan-2-ylacetyl chlorides (XXIII) [42] have the open structure, whereas 2-benzyldimedon-2-ylacetyl chloride [103], in which conjugation of the keto-groups with the aromatic ring is absent, has the cyclic structure (XXIV).

Chlorides of δ-Aldehydo- and δ-Keto-carboxylic Acids (IId–g)

These compounds have been insufficiently studied [104]. The action of thionyl chloride on γγ-dimethyl-δ-oxo-δ-phenylvaleric acid yields a mixture of chlorides of open and cyclic structure [105]. The chlorides of the acids (XVIIIb, c) and (XIXc, d) have the cyclic structure (XXV) and (XXVI) [82,83].



(XXV) (XXVI)

$\nu_{C=O}$ 1750 cm^{-1} (CCl_4) $\nu_{C=O}$ 1770 cm^{-1} (CCl_4)

8-Acylnaphthoyl chlorides [57,87] have the cyclic structure (IIg–B), whereas chlorides of o'-acylbiphenyl-o-carboxylic acids [57] have the open structure (IIh–A).

IV. AMIDES AND HYDRAZIDES

Amides and Hydrazides of γ-Aldehydo- and γ-Keto-carboxylic Acids (IIIa–c)

Amides of aldehydo- and keto-carboxylic acids, whether unsubstituted or substituted on the nitrogen atom, are more stable than the acids themselves, which in solution undergo the tautomerisation IA ⇌ IB. There are a few reports [37,106–108] that the tautomeric equilibrium IIIA ⇌ IIIB is established in solution, but in most cases both isomeric forms (IIIA) and (IIIB) are stable in neutral solvents at room temperature. Aldehydo- and keto-amides are most often obtained only in a single form—(IIIA) or (IIIB)—and only rarely can both isomers be isolated [99,106,109–113].

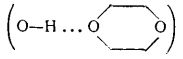
‡Infrared bands (cm^{-1}) of solutions in dioxan. Integrated intensities in practical units of measurement 10^4 M^{-1} cm^{-2} (ln) indicated in parentheses.

The true structure of β-acylpropionamides and o-benzoylbenzamides could not be established by chemical methods. Erroneous conclusions were reached also from polarographic examination [114], the use of which to establish the structure of compounds capable of isomeric or tautomeric conversions requires caution [115]. The structures of these compounds, first prepared long ago, have since been refined by spectroscopic methods [102,106,116–118].

Infrared spectroscopy is most often used to establish reliably the structures (IIIA) and (IIIB) (general frequency data will be found in Refs. 99 and 106). The main evidence of the open structure (IIIA) in N-monosubstituted keto-amides is the presence [55,99,106,110,117,119,120] of the amide-II band (νC-N + δN-H) at 1570–1520 cm^{-1}. In the spectra of the crystalline compounds [99,120], moreover, comparatively narrow N—H bands at 3500–3150 cm^{-1} (IIIA) are easily revealed and distinguished from the broad O—H bands (IIIB) in the same region. Because of angular strain of the >C=O bonds in the five-membered ring the C=O band of the lactam in the spectra of solutions of (IIIa–c–B) is shifted to higher frequencies than the amide-I band in the spectra of the open isomers (IIIa–c–A). The integral intensities of these bands have been measured [91,100,101,103,109,110,121].

The use of carbonyl bands to establish the structure of crystalline keto-amides is complicated by the presence of stable intermolecular hydrogen bonds O–H...O=C (lactam) in the lattice of the cyclic isomers (IIIB). [17,55,99–103,110,121] This displaces the carbonyl band to lower frequencies (than in the spectra of solutions) or even splits it into two bands representing absorption by bound and by free C=O groups. The band due to a bound carbonyl group in the spectra of crystalline o-benzoylbenzamides, which actually have the cyclic structure [99,102,106,118], was wrongly accepted [98] as the total band (νC=O ketone + νC=O amide) in the form (IIIb–A). This led to the erroneous conclusion [27,98] that these amides have the open structure in the crystalline state. For the same reason the infrared spectra of crystalline cis-β-aroylacrylamides were wrongly interpreted [122].

The frequencies and intensities of the carbonyl bands of hydroxy-lactams (IIIB) must be measured in dioxan. As a result of the formation of intermolecular hydrogen bonds with the solvent

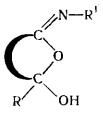


only the absorption due to free carbonyl groups is observed in the spectrum. A shift to lower frequencies, increase in intensity, and splitting of the carbonyl bands in the spectra of hydroxy-lactams (IIIB) due to intermolecular hydrogen bonds have been observed [110,118] also in solvents of low polarity. They were incorrectly explained [119] by the equilibrium IIIA ⇌ IIIB.

The infrared spectra of crystalline amides having the open structure (IIIA) exhibit [35,55,99,110] a decrease in frequency and splitting of the amide-I band with an increase in frequency of the amide-II band. This indicates the presence of intermolecular hydrogen bonds N–H...O=C (in the amide). Complications in interpreting the infrared spectra of the open isomers (IIIA) in solution sometimes arise from the coalescence of the two carbonyl bands (ketone and amide) [55,56,99,117,119]. In such cases it is advisable to measure the integrated intensity of the whole band [99]. It has been possible in this way to explain the infrared spectra of o-benzoyl-N-t-butylnitrobenzamides [56]. In these spectra the two carbonyl bands appear together and, furthermore, the amide-II band overlaps the band due to antisymmetric stretching vibration of the nitro-group.

In addition to infrared spectroscopy, ultraviolet spectroscopy [6,51,107,117,119,123-125], proton magnetic resonance spectra [37,106,108,111-113,119,123,124], and mass-spectrometric data [113] have been used to establish the structure of keto-amides.

It has recently been reported [108] that the presence of a third tautomeric form



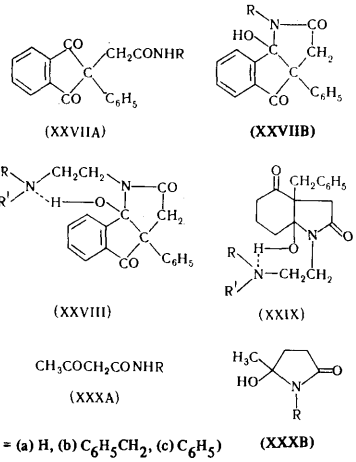
(IIIC)

in solutions of $\beta\beta$-dimethyl-γ-oxovaleramides [125] has been confirmed by proton magnetic resonance. However, formation of this isomer is improbable, so that more rigorous proof, using different spectroscopic methods, is necessary for its confirmation.

Formation of the cyclic modification of keto-amides (IIIB) is favoured by factors tending to make the ketonic carbon atom more strongly electrophilic, make the nitrogen atom more strongly nucleophilic, and bring the two groups closer together in space. *N*-Unsubstituted β-formyl-β-R-butyramides have the ring structure [126,127]. β-Acylpropionamides have either the cyclic or the open structure depending on the substituent R attached to the keto-group and the substituent R′ on the nitrogen atom, and also on the presence or absence of alkyl substituents on the chain carbon atoms [48,50,93,106,111-113,116,117,119-121,124,128-138].

Chiron [119] has found that, among a broad group of β-aroylpropionamides, only the *N*-methylamides§ have the ring structure, which he explains by hyperconjugation. Another explanation has been suggested [139]: the stability of the cyclic form improves with increase in the $+I$-effect of the substituent R′ on the nitrogen atoms ($H < CH_3 < C_2H_5 <$ iso-C_3H_7). On the other hand, increase in the effective steric volume of R′ destabilises the ring form [48,99,110,140]. Aggregating these effects—electronic and steric—may lead to enhanced stability of the cyclic forms of *N*-methylamides. As would be expected, the introduction of methyl groups at the α and β carbon atoms in β-acylpropionamides improves the stability of the cyclic forms [120,124].

Both isomers stable in solution were first obtained [110,141] in a series of *N*-alkyl-1,3-dioxo-2-phenylindan-2-yl-acetamides (XXVIIA) and (XXVIIB). The isomerisation XXVIIB → XXVIIA is accomplished by heating [37,106], and the isomerisation XXVIIA → XXVIIB by the catalytic action of bases. Owing to thermal isomerisation several hydroxylactams (XXVIIB) have two melting points: i.e. after fusion the substance crystallises again, and then melts at the melting point of the corresponding open isomer (XXVIIA). Sometimes it is quite impossible to determine the true melting points. The presence of bulky s- or t-alkyl groups on the nitrogen atom prevents the isomerisation XXVIIA → XXVIIB. [48] The cyclic forms of the *N*-2-dialkylaminoethylamides (XXVIII) and (XXIX) are stabilised by an intramolecular hydrogen bond [109,121,142].



(XXVIIA) (XXVIIB)

(XXVIII) (XXIX)

CH_3COCH_2CONHR

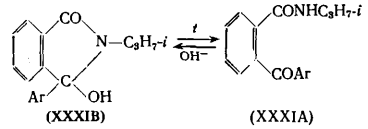
(XXXA)

(R = (a) H, (b) $C_6H_5CH_2$, (c) C_6H_5) (XXXB)

Both isomers have been isolated in the case of the γ-oxovaleramides (XXXa) [106], (XXXb) [111,112], and (XXXc) [113]. Flitsch [106] used proton magnetic resonance to detect the equilibrium A ⇌ B in a solution of the amide (XXXc–A) in hexadeuteriated dimethyl sulphoxide. Later Prelog [113], having isolated both isomers (XXXc–A) and (XXXc–B), established that they were stable at room temperature in the crystalline state and in neutral solvents. Equilibrium was observed between the two forms in the presence of acidic (trifluoroacetic acid) or basic (pyridine) catalysts and also on the surface of silica gel. Isomerisation of the open into the ring form (XXXc–A → XXXc–B) was effected by passing a solution in chloroform through a column packed with an acid ion-exchange resin (Dowex-50W).

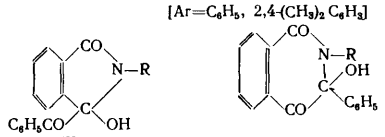
N-Monosubstituted and unsubstituted *o*-formylbenzamides [97,106,111,143,144] and *o*-acylbenzamides [50,51,55,56,99-102,106,111,118,145-152] exist, both in the crystalline state and in solution, in the cyclic form as 3-hydroxy-3-R-2-R′-isoindolinones. Exceptions are *N*-t-alkyl-*o*-acylbenzamides [55,56,99,100] and unsubstituted and *N*-substituted *o*-2′,4′,6′-trimethylbenzoylbenzamides [55], which have the open structure because of steric shielding of the nitrogen atom or the ketonic carbon atom, and are incapable of the transition IIIA → IIIB under the conditions of basic catalysis.

3-Aryl-3-hydroxy-2-isopropylisoindolinones (XXXIB) isomerise thermally into the *N*-isopropylamides (XXXIA) [55,99]. The reverse isomerisation is effected by the action of bases. Increase in the bulk of the substituent on the nitrogen atom facilitates the isomerisation B → A, for thermal isomerisation cannot be achieved in the case of 2-n-alkyl-3-hydroxy-3-phenylisoindolinones [99].



(XXXIB) (XXXIA)

[Ar = C_6H_5, 2,4-$(CH_3)_2C_6H_3$]

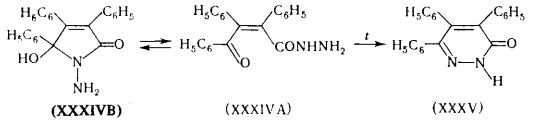


(XXXII) (XXXIII)

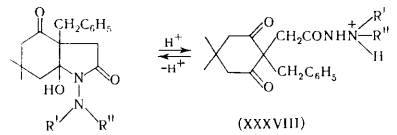
Amides of benzil-*o*-carboxylic acid [101] have been obtained in the cyclic forms (XXXII) and (XXXIII). The six-membered rings are easily isomerised into the more stable five-membered forms (XXXIII → XXXII).

§This relates to *N*-methylamides only of those acids in which the substituted aromatic ring does not possess a strong $+C$-effect.

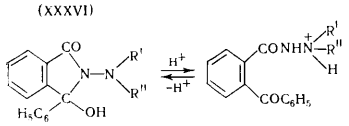
All known *cis*-β-acylacrylamides, whether *N*-substituted or unsubstituted, have the cyclic structure of 5-hydroxy-5-R-1-R′-$\Delta^{3,4}$-pyrrolin-2-ones both in the crystalline state and in solution [6,17,75,123,125,153–159]. Conclusions on the open form of the amides [122,156,160–162] need to be reconsidered.



(XXXIVB) (XXXIVA) (XXXV)

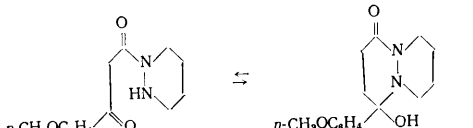


(XXXVI) (XXXVIII)

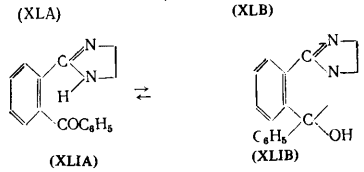


(XXXVII) (XXXIX)

cis-β-Benzoyl-αβ-diphenylacrylohydrazide [75], which has the cyclic structure (XXXIVB), is converted thermally into the dihydro-oxopyridazine (XXXV). *N′N′*-Dialkyl-1,3-dioxo-2-phenylindan-2-ylacetohydrazide (XXVII: R = NR′R″) have been obtained in both isomeric forms A and B [107]. Their interconversion has been accomplished. It is curious that isomerisation of the open into the ring form is effected merely on boiling solutions in ethanol by the autocatalytic action of the basic group NR′R″. Slow establishment of the equilibrium A ⇌ B was observed in solution. *N′N′*-Dialkylhydrazides of 2-benzyldimedon-2-ylacetic and *o*-benzoylbenzoic acids [104] have the cyclic structure (XXXVI) and (XXXVII). When the dialkylamino-group is protonated, the strong $-I$ effect of the substituent on the nitrogen atom effects ring opening with formation of the protonated hydrazides (XXXVIII) and (XXXIX). Deprotonation is accompanied by the reverse process.



(XLA) (XLB)

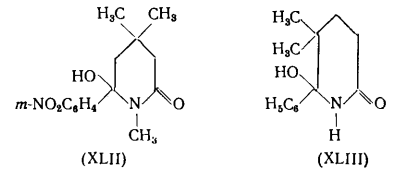


(XLIA) (XLIB)

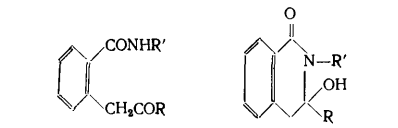
Little study has been made of the structure of *NN′*-dialkylhydrazides of γ-keto-carboxylic acids, where a six-membered ring may be formed. The open form (XLA) predominates [163] in the case of the hexahydropyridazide of β-*p*-methoxybenzoylpropionic acid. The tautomerism XLIA ⇌ XLIB is observed [164] in solutions of *o*-benzoyl-benzamidine.

Amides of δ-Keto-carboxylic Acids (IIId–g)

Spectroscopic examination of a wide range of γ-acyl-butyramides, their *N*-monosubstituted derivatives [120,165], and amides of more complex δ-keto-carboxylic acids [35] has shown that they all have the open structure (IIIA). Only two δ-keto-amides, with a chain of three sp^3 carbon atoms between the carbamoyl and ketone groups, are known in the ring form (XLII) [120] and (XLIII) [166]; both compounds have *gem*-dimethyl groups.



(XLII) (XLIII)



(XLIVA) (XLIVB)

(R=C_6H_5, R′=iso-C_3H_7; R=*p*-$CH_3OC_6H_4$, R′=C_2H_5, *n*-C_3H_7, *n*-C_4H_9, $C_6H_5CH_2$) (R=C_6H_5, R′=CH_3, C_2H_5, *n*-C_3H_7, *n*-C_4H_9, $C_6H_5CH_2$; R=*p*-$CH_3OC_6H_4$, R′=CH_3)

N-Monosubstituted *o*-phenacylbenzamides [139,167,168], with the exception of the *N*-isopropylamide, have the ring structure (XLIVB). Among *o*-*p*′-methoxyphenylbenzamides, in which the ketonic carbon atom becomes less strongly electrophilic under the influence of the +*C*-effect of the methoxy-group, only the *N*-methylamide has the cyclic structure (XLIVB). The isomers (XLIVA) and (XLIVB) are stable in solution. Among *N*-monosubstituted *o*-acylphenylacetamides (IIIf) α-*o*-benzoylphenyl-α-phenylacetanilide has been prepared [169], and exists in the open form.

The structure of the amides (IIIg, h) has not been studied, but it may be supposed that the amides (IIIg) will have the cyclic structure, and (IIIh) the open structure.

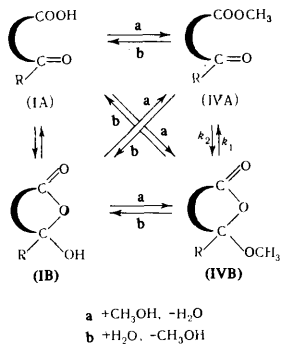
V. ESTERS

Esters of β-acylpropionic [18,22,94,170], *o*-acylbenzoic [27,31,34,51,52,57,61,98,171–175], *cis*-β-acylacrylic [6,7,13,19,21,69,74,75,176–178], and δ-keto-carboxylic [30,82,83,179,180] acids are obtained both in open (IVA) and in cyclic (IVB) forms. Both isomers are stable in neutral solvents at room temperature. The equilibrium IVA ⇌ IVB is established in acid and alkaline media [52,74,94,171] or on heating [177]. Isomers are identified by ultraviolet spectroscopy [7,22,31,34,69,125,177], infrared spectroscopy [7,13,21,22,27,30,34,51,58,69,70,75,82,83,98,171,177], and proton magnetic resonance [21,22,30,31,52,69,70,92,171,177,181], and are determined by gas–liquid chromatography [171], infrared spectroscopy [34], and proton magnetic resonance [31,52,171].

Methods are known [1] for esterifying keto-carboxylic acids to obtain predominantly a certain isomer. Open isomers are formed by the action of alkyl halides on the silver salts [7,25,69] or by esterification of the acids with diazomethane [7,22,30,34,69,75,82,177]. Exceptions have been observed [83] in the latter reaction. Beška [177] found that the esterification of β-formyl-αβ-dihalogenoacrylic acids with diazomethane at 0°C yields predominantly the open isomers, but at higher temperatures the proportion of cyclic isomers in the reaction mixture increases. Thermal isomerisation IVA → IVB of the open esters of these acids has been accomplished. Esters of open structure are obtained by esterifying *o*-formyl- and *o*-acetyl-benzoic acids with methyl iodide in the presence of potassium carbonate [174,182].

Cyclic esters are formed predominantly by the alcoholysis of chloro-lactones (IIB), which is usually conducted in the presence of pyridine [6,7,27,51,57,75,82,83,98,170,180], though urea has also been suggested [183] as base. Cyclic γ-oxovaleric esters are obtained by the alcoholysis of α-angelica lactone [170].

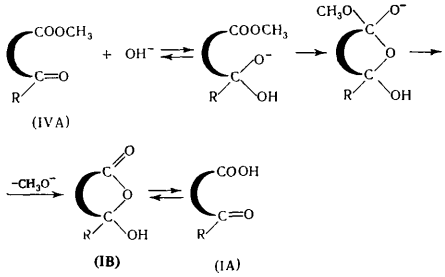
Scheme 2



a +CH_3OH, -H_2O
b +H_2O, -CH_3OH

The esterification of keto-carboxylic acids by alcohols in the presence of hydrogen chloride (Fischer–Speyer method) or other acid catalysts usually leads to mixtures of the two isomers. Their content in the mixture depends on the duration of the reaction (kinetic or thermodynamic control) and is determined by the equilibria [31,52,171,184] in Scheme 2 (intermediate stages not indicated). This scheme shows the possibility of nucleophilic attack at both electrophilic carbon atoms in the molecules (IA) and (IB). Kinetic investigations show [173,174,178,185–191] that a neighbouring carbonyl group accelerates the hydrolysis of esters (IVA). The reason for this effect is that the nucleophilic reagent first attacks the ketonic carbon atom, and the mechanism of alkaline hydrolysis is represented by Scheme 3.

Scheme 3



In thermodynamically controlled Fischer–Speyer esterifications, in the presence of a large excess of methanol, the equilibrium IVA ⇌ IVB plays a decisive role in determining the isomeric composition of the products. Bowden [171] has studied this reversible isomerisation of methyl *o*-acylbenzoates (IVb: R = CH_3, C_2H_5, iso-C_3H_7, t-C_4H_9, $C_6H_5CH_2$, and C_6H_5) under conditions of acid and alkaline catalysis. The equilibrium constants (K = [IVB]/[IVA] = 1.7–8.1 with R = Alk and 0.02 with R = C_6H_5) are almost equal for acid and alkaline catalysis. They increase with the size of the substituent R (CH_3 < C_2H_5 < < iso-C_3H_7 < t-C_4H_9). The explanation is that a bulky substituent destabilises the open form, since the COR group is forced out of the plane of the aromatic ring [43]. The equilibrium constants correlate with the Taft steric constants E_S of the substituents ($\delta = -0.35 \pm 0.05$). The isomerisation rate constants k_1 and k_2 (rates of formation of IVA and IVB) have been measured under conditions of acid catalysts, and are found to fall with increase in the volume of the substituent R, while $k_2 > k_1$. Increase in the volume of R has a greater effect on k_1 than on k_2 (δ = 0.9 and 0.5 respectively).

Unfortunately, such detailed investigations are lacking for esters of other keto-carboxylic acids. However, the equilibrium constant of the reversible isomerisation of keto-carboxylic esters and the tautomeric equilibrium constant K_T of the free acids are determined in general by the same structural factors. There is thus a correlation between the predominant tautomeric form of keto-carboxylic acids and the predominant isomer in the products of thermodynamically controlled Fischer–Speyer esterifications [31]. This explains the preferential formation of open isomers (IVA) in the esterification of γ-oxovaleric [94,170], *o*-aroylbenzoic [27,31,34,52,57,173], *cis*-β-aroylacrylic [21,178], and γ-benzoylbutyric [180] acids. *o*-Acylbenzoic (Ib: R = H, Alk) [20,31,171], *cis*-β-acylacrylic (Ic: R = H, Alk) [69,176,177], and 8-acetylnaphthoic [30] acids, for which the tautomeric equilibrium IA ⇌ IB is displaced towards the cyclic form, on esterification yield predominantly the ring isomers (IVB). The isomerisations IVA → IVB (*cis*-β-formylacrylic esters [177]) and IVB → IVA (γ-oxovalerates [94,170], *o*-aroylbenzoates [51], and *cis*-β-aroylacrylates [7,74]), catalysed by acids or alkalis, are explained by displacement of the equilibrium IVA ⇌ IVB towards the thermodynamically more stable isomer.

VI. MIXED ANHYDRIDES

Mixed anhydrides of keto-carboxylic acids (VA) and their more frequently encountered cyclic isomers—acyloxy-lactones (VB)—are easily identified by infrared spectroscopy. The infrared spectra of the former (VA) are characterised by anhydride carbonyl bands at ~1820 and 1750 cm^{-1} and carbonyl absorption of the aldehydo- or keto-group at 1725–1660 cm^{-1}. Absence of absorption in the range 1725–1660 cm^{-1} is the main evidence for the ring structure (VB). The infrared spectra of (Va–c–B) contain a lactonic carbonyl band at 1810–1775 cm^{-1} and a carbonyl band of the acyloxy-group at 1770–1745 cm^{-1}; [7,22,25,35,69,75,192] sometimes the two bands overlap [35].

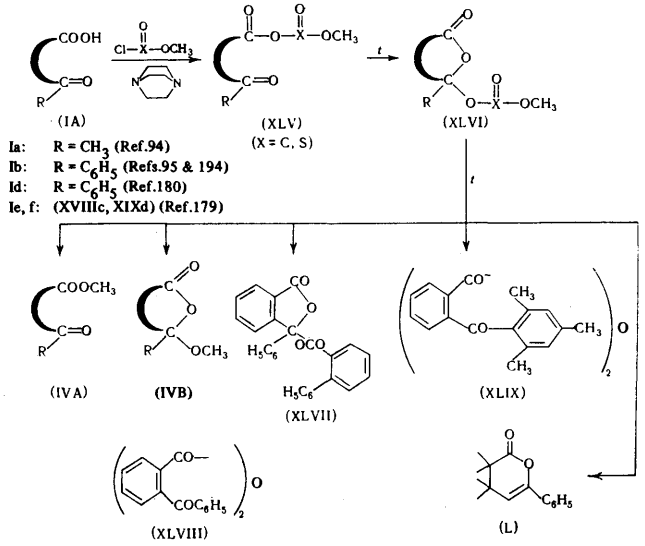
The acylation of β-formylpropionic [22], *o*-acylbenzoic [35,57,59,192,193], *cis*-β-acylacrylic [7,25,69,75,176], and α-*o*-benzoylphenyl-α-methylpropionic [84] acids by means of acetic anhydride [22,59,69,176,193] or mixtures of the anhydride with pyridine [35,57,75,84,192], sodium acetate [192], acetic acid in the presence of sulphuric acid [7], or acetyl or benzoyl chloride [25] gives acyloxy-lactones (VB). A specific method for their preparation is the reaction of cyclic chloro-anhydrides (IIB) with silver acetate [7,193].

Mixed anhydrides of open structure (VA) are obtained by the action of a keten on β-formylpropionic acid [22], by the acetylation of β-benzoyl-αβ-diphenylpropionic acid with acetic anhydride [75], and by the action of acetyl chloride on silver benzil-*o*-carboxylate [193].

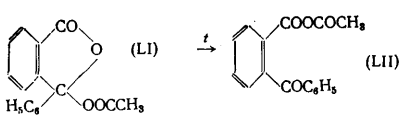
Newman [94–96,180,194] prepared mixed anhydrides of γ- and δ-keto-carboxylic acids (XLV) by the action of methyl chloroformate or chlorosulphite on the acids in the presence of a base, 1,4-diazabicyclo[2,2,2]octane, or directly on their sodium salts.

Heating converts the mixed anhydrides (XLV) into the cyclic isomers (XLVI) (not in all cases isolated). At higher temperatures the latter undergo pyrolysis to form a mixture of esters (IVA) and (IVB). Pyrolysis of the mixed anhydride (XLV: X = C) obtained from *o*-benzoylbenzoic acid yields not only IVA and IVB but also *o*-benzoylbenzoyl anhydride (XLVII), in which one acid radical has the cyclic structure, and the other the open structure. The anhydride (XLVII) is obtained also by the action of ethoxyacetylene on *o*-benzoylbenzoic acid, by the reaction of 3-chloro-3-phenylphthalide (IIb–B: R = C_6H_5) with *o*-benzoylbenzoic acid in the presence of pyridine [95], and by the action of sodium nitrite on 3-chloro-3-phenylphthalide [98]. The structure (XLVIII) (Scheme 4) had previously been attributed to the anhydride (XLVII) on the basis of ultraviolet spectroscopy [193] and polarographic results [195]. Pyrolysis of the mixed anhydride of *o*-2′,4′,6′-trimethylbenzoylbenzoic acid (XLV: X = C) gives as sole product the anhydride (XLIX). The mixed anhydrides of γ-benzoylbutyric acids and their *gem*-dimethyl derivatives yield unsaturated lactones (L) as well as the corresponding esters (IVd–B).

Scheme 4



Schmid [193] showed that 3-phenylphthalid-3-yl acetate (LI) undergoes thermal isomerisation into the mixed anhydride (LII):



in the opposite direction to that of the mixed anhydrides of methoxyformic acid studied by Newman.

Published information does not reveal the effect of the structure of the acyl residue (the substituent R′ in formula V) on the stability of the mixed anhydrides (VA) and (VB) or the conditions of their isomeric interconversion.

ADDENDUM

Several papers were published while this Review was being prepared for the press, and are briefly surveyed below.

The electronic and steric effects of substituents near the keto-group and in the ring on the position of ring–chain tautomeric equilibrium in a series of aromatic *o*-ketocarboxylic acids have been discussed [196]. The relative reactivities of ring and chain isomers of α-*gem*-disubstituted β-formylpropionic acids and their esters have been studied [197].

The presence of an intramolecular hydrogen bond has been established [198] in *N*-aryl-β-aroylpropionamides. A study has been made of the chemical properties of several *m*-acylbenzamides existing in the ring form [199,200]. Both isomers (IIIA and IIIB) of the 3,4-dimethoxyphenethylamide of 3-oxocycloheptanecarboxylic acid have been isolated [201].

A review [202] lists papers on the use of nuclear magnetic resonance spectroscopy for the study of ring–chain tautomeric phenomena.

Structure and ring–chain isomerism have been studied in amides of β-formylpropionic [203,204] and $\beta\beta$-dimethyl-γ-oxovaleric [205] acids. Both isomers of phenyl *o*-benzoylbenzoate have been prepared [206]. The cyclic isomers of *cis*-β-formylacrylic acids exhibit an extraordinarily strong tendency to associate [207].

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Chemistry Faculty,
Riga Polytechnic Institute

U.D.C. 547.454

The Synthesis of Unsaturated Carbohydrates

Yu.A.Zhdanov and V.G.Alekseeva

The review deals with modern achievements in the chemistry of unsaturated carbohydrates. The methods of synthesis of these compounds, their use for the preparation of compounds of other classes, and in a few cases their properties have been analysed. A systematic account is given of the available data on the basis of the method employed, i.e. on the basis of the reactions used to form multiple bonds. The methods for the elimination of various groups, Grignard syntheses, the Knoevenagel - Doebner condensation, and the Wittig reaction are analysed in succession. Considerable attention has been devoted to the discussion of conformational effects and reaction mechanisms.
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I. INTRODUCTION

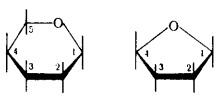
The chemistry of unsaturated monosaccharides has now become an extensive and fairly independent branch of carbohydrate chemistry. The interest in these sugar derivatives is due to the fact that their reactions constitute the basis of convenient methods for the synthesis of many biologically important compounds—deoxy- and amino-sugars, sialic acids, nucleosides, branched carbohydrates, sphingosines, etc.[1,2] Derivatives of unsaturated monosaccharides have been isolated from natural raw materials both in a free form (ascorbic and shikimic acids)[3] and as components of antibiotics (angustmycin[4], blasticidin[5]). Unsaturated carbohydrates are actively involved in the metabolism of the living cell, since the biosynthesis of aromatic compounds is associated with their various reactions[6]. Moreover, it has been shown recently that unsaturated monosaccharides play an important role in the acid and alkaline degradation of carbohydrates[7].

Many methods of synthesis of unsaturated monosaccharides are known at present. (We have covered the literature up to October, 1970, inclusive.) The aim of the present review is a systematic account of experimental data on the basis of reaction types and not the classes of unsaturated carbohydrates as in previous reviews[1,2]. This makes it possible to consider the problem from the standpoint of the general characteristics of organic synthesis.

The most modern carbohydrates nomenclature[8], proposed in 1963, is largely employed in the review, although trivial names are sometimes used.

II. STRUCTURAL TYPES AND STRUCTURE OF UNSATURATED CARBOHYDRATES

The unsaturated carbohydrates known at present can be divided into two independent groups in accordance with their structural features: cyclic and acyclic compounds. The first group has a greater variety of structures. It includes compounds with endo- and exo-cyclic double bonds. Pyranose (I) and furanose (II) structures are known with all possible types of location of the endocyclic double bond, i.e. $\Delta^{1,2}$-, $\Delta^{2,3}$-, $\Delta^{3,4}$-, and $\Delta^{4,5}$-derivatives (compounds of the last type are naturally only pyranose derivatives). $\Delta^{1,2}$-Derivatives are usually called glycals. $\Delta^{1/2}$-Derivatives of pyranoses and furanoses and also $\Delta^{3,4}$-derivatives of furanoses and $\Delta^{4,5}$-derivatives of pyranoses are essentially cyclic vinyl ethers. In compounds with an exocyclic double bond, the latter either adjoins directly the ring [compounds (III)] or is separated from it by one or several carbon atoms [compounds (IV)].

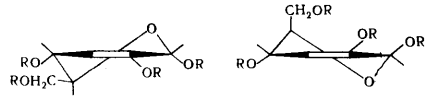


(I) (II)

R=CHR' (III) R = (I) or (II)
RCH=CHR' (IV) R' = H, Alk.

The following classes may be distinguished among unsaturated acyclic carbohydrate derivatives: polyols[1], aldehydo-forms[9], hydrazones[10], nitroalcohols[1], sulphones[11], keten dithioacetals[12], and aldonic[13] and glycaric acids[14].

Since unsaturated carbohydrates contain trigonal carbon atoms (sp^2-hybridisation), their conformations are distorted compared with the usual sugars. This is because the ethylene carbon atoms and two adjacent carbon atoms must be in the same plane. On the basis of general considerations[15], the half-chair conformations H1 and 1H are the most probable for the cyclic unsaturated carbohydrates of types (I) and (II). Recently NMR spectroscopic studies have been begun in order to establish the exact conformations of unsaturated sugars[16-19]. In particular, on the basis of the large coupling constant $I_{4,5}$ (6—10 Hz) for α-anomers of various derivatives of 3-deoxy-D-*erythro*-hex-2-enopyranose, Ferrier[18] suggested the occurrence of H-4 and H-5 diaxial interactions. From this it follows that the above compounds exist preferentially in the H1 conformation (V). β-Anomers of the same carbohydrate derivatives have low values of $I_{4,5}$ (1.5—2 Hz) and therefore are more likely to have the 1H conformation (VI):

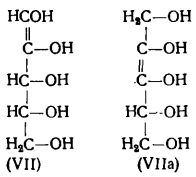


(V) (VI).

(R = Ac, Bz)

The results obtained are consistent with the general hypothesis[6] concerning the relative stabilities of the conformations of the α- and β-anomers (the anomer effect).

In a study and interpretation of the reactivities of unsaturated carbohydrates, account must be taken, together with steric factors, also of the distribution of electron density over their carbon atoms. The first attempt to perform a quantum-mechanical calculation of electron distribution in the molecules of unsaturated carbohydrates was made by Zhdanov and coworkers[20,21]. The results of calculations on endiols of types (VII) and (VIIa) show appreciable positive σ charges on the carbon atoms of the double bond. Structure (VII) may be regarded as analogous to that of a glycal for which attack by a proton on the second carbon atom is typical in electrophilic addition reactions. This may be explained by the fact that the π electron cloud, which interacts initially with the proton, is displaced to the $C_{(2)}$ atom with its high positive charge:



(VII) (VIIa)

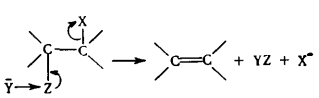
III. METHODS OF SYNTHESIS OF UNSATURATED SUGARS

There are two fundamentally different methods for synthesising unsaturated carbohydrates. These are firstly the elimination of various groups from substituted monosaccharides—the classical procedure for the formation of a double bond. Such reactions do not of course involve a rearrangement of the carbon skeleton of carbohydrates. The second method is based on a wide variety of condensations involving the carbonyl group of sugars which take place with a simultaneous increase in the length of the carbon chain.

1. ELIMINATION REACTIONS

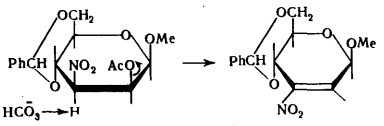
a. $\alpha\beta$-Elimination

Most elimination reactions leading to the formation of unsaturated sugars proceed via an $\alpha\beta$-elimination mechanism:

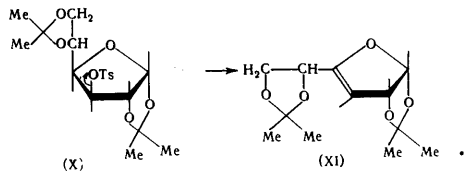


(X = OAc, OTs, OBz; Z = H, Hal).

The E_2 synchronous elimination mechanism, which reduces to a single-stage reaction of a base (Y^-) and the carbohydrate molecule, is the most probable. The most important condition for such eliminations is known to be a *trans*-diaxial disposition of the X and Z groups to be eliminated. Hence it follows that the E_2 mechanism occurs most frequently in rigid cyclic systems. Thus the elimination of acetic acid from the cyclic nitropyranoside (VIII) takes place readily[22,23] in the presence of a weak base such as sodium bicarbonate with a yield of 70—80%. In this case, elimination is evidently facilitated not only by the *trans*-diaxial disposition of the groups eliminated but also by the presence of the nitro-group which increases the acidity of the proton at $C_{(3)}$.

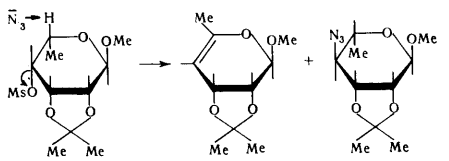


(VIII) (IX)



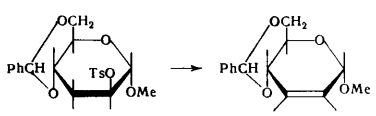
(X) (XI)

When there is no activation of this type, stronger bases are required: soda-lime, alkoxides, and azides. For example, on heating with soda-lime, the furanose (X) is converted[24] into 1,2:5,6-di-*O*-isopropylidene-3-deoxy-α-D-*erythro*-hex-3-eno-1,4-furanose (XI) and treatment of methyl 6-deoxy-1,2,3-*O*-isopropylidene-4-*O*-methanesulphonyl-α-L-talopyranoside (XII) with sodium azide yields[25] an unsaturated product (XIII) together with the azide (XIV) in proportions of 3:1 respectively:

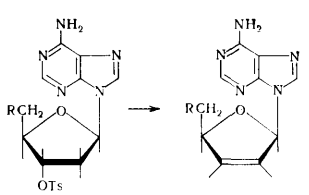


(XII) (XIII) (XIV)

In this case the deoxy-unit serves as the proton donor; other similar examples may be quoted[26,27]:



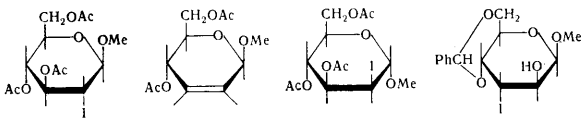
(XV) (XVI)



(XVII) (XVIII)

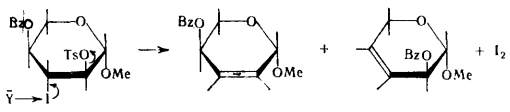
The elimination reaction where the first stage is the elimination of the halide ion (Z = Hal, left column) is also frequently used to form a double bond in the carbohydrate molecule. Thus when the pyranoside (XIX) was treated with $NaCo(CO)_4$, the product was methyl 4,6-di-*O*-acetyl-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranoside (XX). The analogous derivative of mannose (XXI) forms a $\Delta^{2,3}$-unsaturated compound under more severe conditions[28] owing to the *cis*-disposition of the groups eliminated. When an attempt was made to obtain the 2-*O*-methanesulphonyl derivative from the pyranoside (XXII) by treatment with

methanesulphonyl chloride in pyridine, methyl 4,6-*O*-benzylidene-β-D-*threo*-hex-2-enopyranoside was isolated[29]:



(XIX) (XX) (XXI) (XXII)

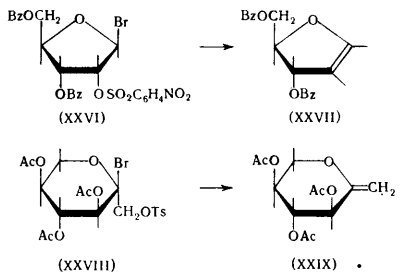
Sodium iodide in acetone is very often employed as the nucleophilic agent for the elimination reaction. Dimitrievich and Taylor[30] obtained by this procedure methyl 4-*O*-benzyl-2,3-dideoxy-β-L-glyceropent-2-enoside (XXIV) from the 3-iodo-derivative (XXIII) and also isolated the side product (XXV). The formation of two isomeric unsaturated sugars (XXIV) and (XXV) can be explained by the allyl rearrangement of the benzyl group in (XXIV) with formation of an equilibrium mixture of the $\Delta^{2,3}$- and $\Delta^{3,4}$-derivatives:



(XXIII) (XXIV) (XXV)

When tosyl derivatives of type (XXVI) are treated with sodium iodide in acetone, an unsaturated sugar (XXVII) and elemental iodine are also formed[31]. In this case the tosyl group is probably replaced by iodine and the resulting iodo-derivative undergoes elimination by the mechanism quoted above.

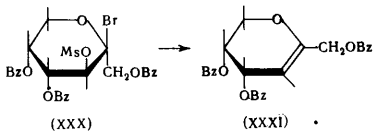
Using this possibility, Ness and Fletcher[31] obtained the furanal (XXVII) from the tosyl derivative (XXVI). Earlier attempts to synthesise (XXVII) by the usual methods for glycals (zinc in acetic acid) proved to be inapplicable owing to the lability of (XXVII) in acid media:



(XXVI) (XXVII)

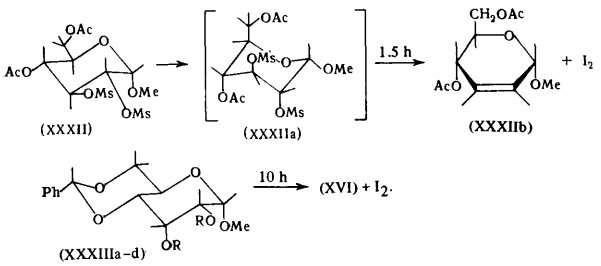
(XXVIII) (XXIX)

Using the method Ness and Fletcher, Tokuyama et al.[32] obtained 3,4,5-tri-*O*-acetyl-1,2-dideoxy-L-*xylo*-hex-1-enopyranose (XXIX) from 3,4,5-tri-*O*-acetyl-1-*O*-(*p*-tosyl)-α-L-sorbopyranosyl bromide (XXVIII). The glycal (XXXI) with an endocyclic double bond was obtained similarly from the bromide (XXX):



(XXX) (XXXI)

In this case, when both groups eliminated are identical (X = Z = OTs, OMs, *p*-$BrC_6H_4SO_2$, or *p*-$NO_2C_6H_4SO_2$), more severe conditions are required for the elimination process. Tipsom and Cohen[34] suggested that a 20% solution of sodium iodide in dimethylformamide (DMF) in the presence of zinc must be employed. The first step in this reaction is probably the replacement by iodine of one of the groups eliminated with formation of an iodide (see above). The latter is attacked by the nucleophilic agent, yielding an unsaturated derivative. Zinc is required to bind the iodine eliminated, which can add under the reaction conditions (boiling DMF) to the unsaturated carbohydrate formed, reducing its yield. Methyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (XXXIIIb) was obtained in this way from methyl 4,6-di-*O*-acetyl-2,3-di-*O*-methanesulphonyl-α-D-*gluco*-pyranoside (XXXII).[35] It is interesting to note that the elimination reaction with 4,6-*O*-benzylidine derivatives (XXXIII, a—d) is much slower[36] than with (XXXII), probably because the presence of the rigid *trans*-junction of two six-membered rings prevents the methanesulphonyl groups from occupying the *trans*-diaxial positions. The 4,6-diacetates (XXXII) can have the $C_{(1)}$-conformation (XXXIIa) at the instant of reaction, where both methanesulphonyl groups are *trans*-diaxial, which of course accelerates the elimination reaction.

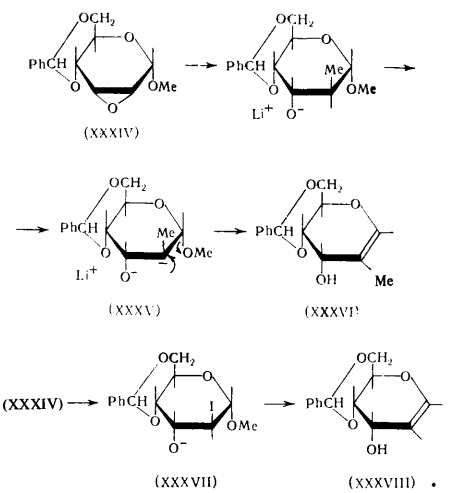


(XXXII) (XXXIIa) (XXXIIb)

(XXXIIIa-d)

(a) R = Ts; (b) R = Ms; (c) R = *p*-$NO_2C_6H_4SO_2$; (d) R = *p*-$BrC_6H_4SO_2$.

Epoxides are frequently used to synthesise unsaturated carbohydrates. *trans*-Diaxial ring-opening products (the Reichstein rule) are probably formed as intermediates in this process and subsequently undergo elimination by the mechanism described above (p. 478). For example, Horton and coworkers[36] treated the epoxide (XXXIV) with potassium ethylxanthate and obtained the $\Delta^{2,3}$-derivative (XVI). On the other hand, the use of methyl-lithium to open the ring of the epoxide (XXXIV) unexpectedly leads to the $C_{(2)}$-substituted glycal (XXXVI),[37-39] instead of the $\Delta^{2,3}$-derivative (XVI). The mechanism of this reaction has not been elucidated. The first stage is probably *trans*-diaxial opening of the epoxide ring with subsequent elimination of a proton from $C_{(2)}$. The resulting dianion (XXXV) is subsequently converted into the glycal (XXXVI) following the loss of a methoxide ion, as shown in the scheme below:

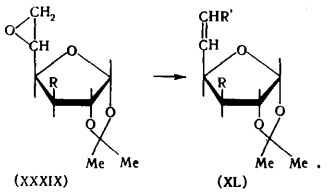


(XXXIV) (XXXV) (XXXVI)

(XXXVII) (XXXVIII)

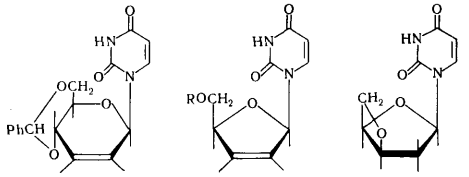
If the methyl-lithium solution contains lithium iodide, the initial epoxide (XXXIV) gives rise initially to the iodohydrin (XXXVII), with subsequent formation of the glycal (XXXVIII).

Methyl-lithium has been successfully used[40] also to open the terminal epoxy-ring of 5,6-anhydro-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucose (XXXIX, R = OBz) to give the unsaturated furanoside (XL, R = OBz, R′ = H):



(XXXIX) (XL)

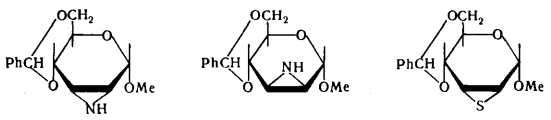
Unsaturated nucleosides (XLI) and (XLII, R = Bz, Tr, or H) have been synthesised by the reaction of epoxides with various nucleophilic agents[41,42]:



(XLI) (XLII) (XLIII)

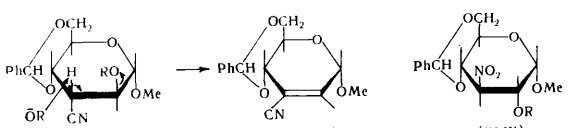
Horwitz et al.[43] described an interesting case of the ring opening of the anhydro-derivative (XLIII) by potassium t-butoxide in dimethyl sulphoxide (DMSO), which is also accompanied by the formation of the unsaturated nucleoside (XLII, R = H).

Together with the reactions of epoxides, the interaction of aziridine compounds of types (XLIV) and (XLV) and of the thi-iron (XLVI) with nucleophilic agents also gives rise to the corresponding unsaturated derivatives[36,44]:



(XLIV) (XLV) (XLVI)

All the reaction discussed above are examples of *trans*-elimination, characteristic of reactions proceeding via the E_2 mechanism. However, since, apart from steric conditions, the elimination reaction is controlled also by electronic factors, cases of *cis*-elimination are likewise possible. They occur mainly when the group eliminated (usually the proton) is activated by an electron-accepting substituent. For example, when an attempt was made to carry out epimerisation at the second carbon atom of the pyranoside (XLVII) with sodium methoxide, the cyano-olefin (XLVIII) was obtained instead of the expected epimer[45]:

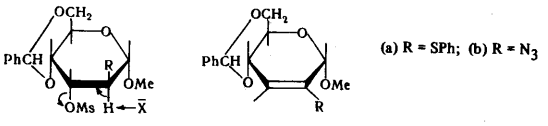


(XLVII) (XLVIII) (XLIX)

(R = H, Ac, Ts)

Despite the *cis*-disposition of the groups eliminated in the nitroglycoside (XLIX), the elimination process can nevertheless be carried out[46-50] albeit under more severe conditions (alumina in boiling toluene) than for the galactose derivative (VIII).

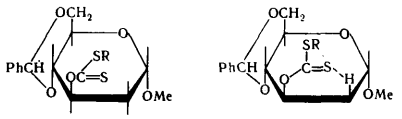
Hanessian[51] described the formation of the vinyl thioether (LIa) from compound (La) and an unsaturated azide (LIb) from (Lb) via *cis*-elimination under the influence of 1,5-diazabicyclo[4,3,0]nonene in dry DMSO. Owing to the large bulk of the nucleophilic agent employed, the competing nucleophilic substitution reaction was ruled out:



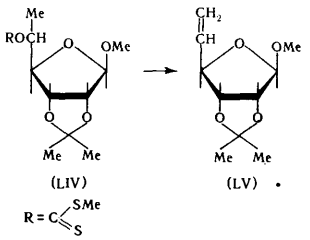
(a) R = SPh; (b) R = N_3

(L) (LI)

A classical example of *cis*-elimination in carbohydrates is the pyrolysis of sugar xanthate esters (the Chugaev reaction). Under these conditions, the hydrogen of the deoxy-units is as a rule involved in the elimination process. Thus the xanthates (LII) and (LIV) yield[52,53] methyl 4,6-*O*-benzylidene-α-D-*threo*-hex-2-enopyranoside (XVI) and methyl 2,3-*O*-isopropylidene-β-D-*ribo*-hex-5-enofuranoside (LV). *cis*-Elimination can be readily accounted for by the formation of a six-membered intermediate transition state (LIII):

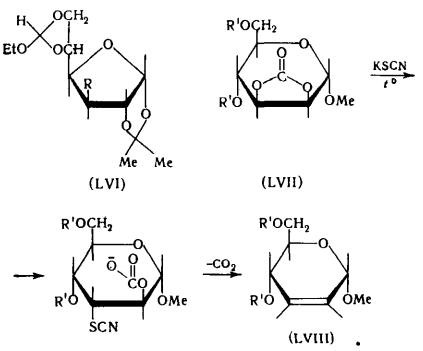


(LII) (LIII)



(LIV) (LV)

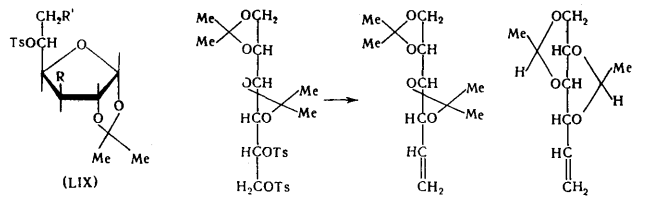
An unusual method for the conversion of a glycol group into a double bond involves the hydrolysis of cyclic orthoformates on heating the latter with acids. The furanoside (LVI) was converted in this way into an olefin (XL, R = OMe, or OCH_2Ph, R′ = H). Klemer and Mersmann[55] employed cyclic sugar carbonates to synthesise unsaturated carbohydrates. By treating methyl α-D-*manno*-pyranoside 2,3-carbonate (LVII) *in vacuo* at 120°C with potassium thiocyanate, they obtained the unsaturated methyl α-D-*manno*-pyranoside (LVIII). According to the mechanism proposed by the authors, in the first stage nucleophilic substitution takes place at $C_{(3)}$ with subsequent formation of (LVIII) and carbon dioxide:



(LVI) (LVII) (LVIII)

(R = H, COOBzl)

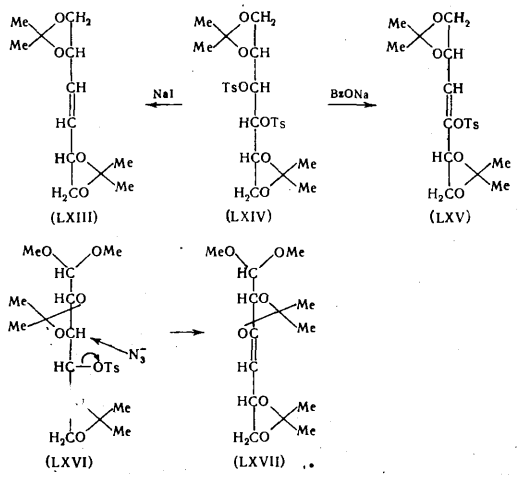
In cyclic systems, the *trans*-diaxial disposition of the groups eliminated, which is necessary for a successful elimination reaction, restricts the choice of the starting compound. Since in acyclic carbohydrate derivatives there is a possibility of free rotation of the substituents about the single carbon—carbon bond, this limitation is removed. In particular 5,6-dideoxy-1,2-*O*-isopropylidene-*α*-D-*xylo*-hex-5-enofuranose (XL, R = OH, R′ = H) and its 3-azido- and 3-*O*-methanesulphonyl derivatives are readily formed[56-58] when 5,6-ditosyl derivatives of type (LIX) are treated with sodium iodide in acetone. The mannitol (LXI) and sorbitol (LXII) derivatives have been synthesised similarly. According to the data of Foster and Overend[59], the reaction mechanism is similar to that quoted on p. 479.



(LIX) (R = OH, N_3, OMs; R′ = OTs, OMs) (LX) (LXI) (LXII).

When 1,3:2,4-di-*O*-ethylidenesorbitol 5,6-dinitrate is employed, an olefin (LXII) is also formed[60]. The initial reaction stage may be the replacement of the primary nitro-group by iodine but this intermediate has not been isolated. It is probably unstable and may be immediately converted into the olefin (LXII).

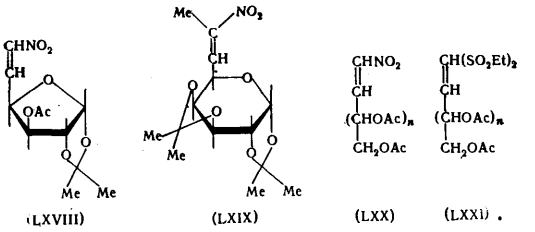
Since the secondary *p*-toluenesulphonyl group is replaced by iodine with considerable difficulty (p. 479), the synthesis of the polyol (LXIII) with a non-terminal double bond from compound (LXIV) requires more severe conditions of the kind used earlier for cyclic ditosyl derivatives of type (XXXIIIa). For example, Tipson and Cohen[34] converted 1,2:5,6-di-*O*-isopropylidene-D-mannitol 3,4-di(toluene-*p*-sulphonate) (LXIV) into 1,2:5,6-di-*O*-isopropylidene-*trans*-hex-3-ene-D-*threo*-1,2,5,6-tetrol (LXIII) by heating (LXIV) with a 20% solution of sodium iodide in DMF in the presence of zinc. Treatment of the product (XLIV) with sodium benzoate in DMF yields[61] an olefin (LXV) having a different structure, the formation of which can be accounted for by the classical E_2 mechanism.



(LXIII) (LXIV) (LXV) (LXVI) (LXVII).

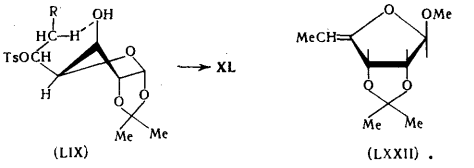
Paulsen[62,63] showed that, in the synthesis of the azide from the 4-*O*-tosyl derivative (LXVI), an unsaturated polyol (LXVII) is formed together with the expected product.

An increase of the acidity of the proton eliminated facilitates the elimination process. Thus the formation[64-71] of unsaturated nitro-compounds (LXVIII), (LXIX), and (LXX) proceeds equally readily regardless of the configuration of the initial carbohydrate. Acetic acid is eliminated even more readily[11,72], from sugar sulphone acetates with formation of a product of type (LXXI):



(LXVIII) (LXIX) (LXX) (LXXI).

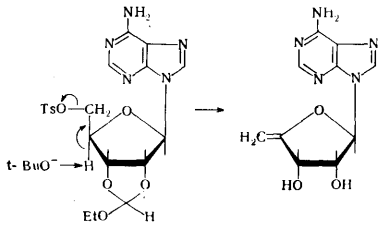
The elimination may be facilitated by the simultaneous involvement of adjacent groups[73-76]. For example, a number of workers[73,75] have shown that in the synthesis of olefins (XL, R = OH, R′ = OBz, H, or OTr) from 5-*O*-tosyl derivatives (LIX, R = OH, R′ = H, Bz, or OTr), the concentration of sodium methoxide employed as a base plays a significant role. In particular, an increase of the concentration of methoxide ions from one to four moles per mole of the initial tosyl derivative (LIX) increases sharply the yield of the olefin (XL). On the other hand, when the substituent at $C_{(3)}$ is resistant to alkalides, the corresponding olefin is hardly formed. All the above remarkable findings can be accounted for by the involvement in the elimination reaction of the hydroxyl at $C_{(3)}$ which facilitates the partial dissociation of the hydrogen atom at $C_{(6)}$, as shown in the scheme below:



(LIX) (LXXII).

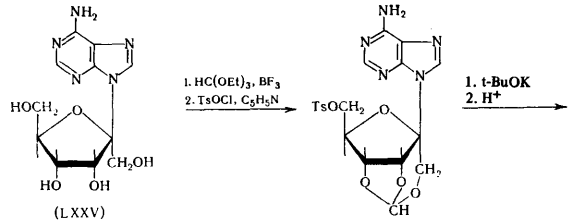
One should expect the elimination of the proton at $C_{(4)}$, but in this case the *trans*-orientation of the proton of the tosyl group is impossible owing to steric hindrance of the substituent at $C_{(3)}$. The reason for the formation[74] of the derivative (LXXII) on treating methyl 6-deoxy-2,3-*O*-isopropylidene-5-*O*-tosyl-*β*-D-*allo*-furanoside (LIV, R = Ts) with alkoxides in hot alcohol is understandable from this standpoint. Here the simultaneous involvement of the hydroxy-group at $C_{(3)}$ is naturally impossible, while, on the other hand, the *trans*-orientation of the tosyl group and of the hydrogen atom at $C_{(4)}$ is quite likely, since the asymetric $C_{(3)}$ atom has the D-configuration. Compound (LXXII) is interesting because it is a structural analogue of the carbohydrate component of the nucleosidic antibiotic decoyinine[4] (XXVI). A closer analogue of decoyinine

(LXXIV) has been synthesised[77] from the 5-*O*-tosyl derivative (LXXIII):

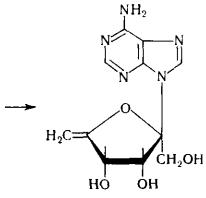


(LXXIII) (LXXIV)

On the basis of these preliminary studies, Robins and coworkers[77] achieved an elegant synthesis of decoyinine (LXXVI) from psicofuranine (LXXV):

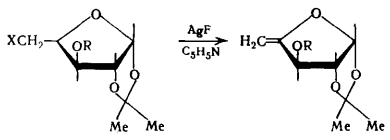


(LXXV)



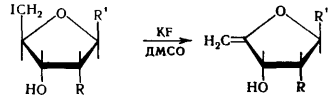
(LXXVI)

5-Halogeno-derivatives (LXXVII, a and b) and (LXXIX) can be employed[78-82], apart from tosyl derivatives, to introduce an exocyclic 4-methylene group:



(LXXVII) (LXXVIII)

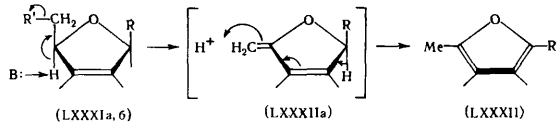
(LXXVIIa), L-configuration at $C_{(4)}$, X = I, R = H
(LXXVIIb), D-configuration at $C_{(4)}$, X = Br, R = Me



(LXXIX) (LXXX)

(a) R = H, R' = thymidyl
(b) R = OH, R' = uridyl

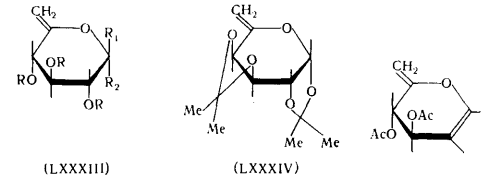
When an attempt was made to carry out a similar reaction[27,83] with unsaturated nucleosides of (LXXXI, a and b), only the furan derivatives (LXXXII) were obtained. Probably the product (LXXXIIa) formed initially readily loses a proton at $C_{(1')}$, yielding a stable nucleoside of type (LXXXII):



(LXXXIa, b) (LXXXIIa) (LXXXII)

(LXXXIa), R = thymidyl, R' = I
(LXXXIb), R = adenyl, R' = H or SEt.

The elimination of hydrogen halides under the influence of silver fluoride in pyridine has been used[1,84] also in the syntheses of numerous unsaturated derivatives of aldoses and aldosides of types (LXXXIII), (LXXXIV), and (LXXXV):

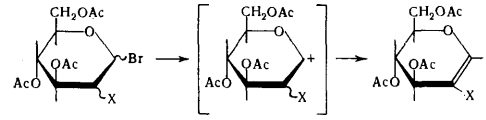


(LXXXIII) (LXXXIV)

(a) R = Ac; R_1 = H, R_2 = OMe;
(b) R = Ac; R_1 = OMe, R_2 = H

(LXXXV).

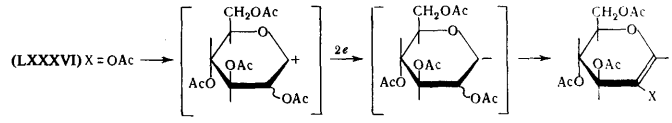
The well known derivatives of 2-hydroxyglycals (LXXXVIII) can be obtained by the elimination of hydrogen bromide from glycosyl bromides under the influence of diethylamine[1]:



(LXXXVI) (LXXXVII) (LXXXVIII).

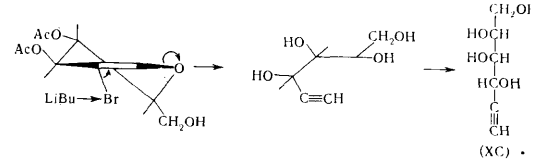
(X = OAc, NO, NO_2, Cl, SCN)

The rate of elimination of hydrogen bromide increases[85] following the addition of polar solvents. This finding is consistent with the E_1 mechanism via the intermediate sugar cation (LXXXVII), which the authors proposed. The elimination of hydrogen bromide from glycosyl bromides of 2-deoxy-sugars can yield an important class of unsaturated hydrocarbons—glycals (LXXXVIII, X = H). However, this reaction is of no preparative value, since the initial 2-deoxyglycosyl bromides are themselves obtained from glycals. The latter are usually synthesised by treating acetohalogenoses (LXXXVII, X = OAc) with zinc dust in acetic acid. As in the synthesis of 2-hydroxyglycals, the dissociation of the initial glycosyl bromide results in this case in the intermediate formation[1,86] of the sugar cation (LXXXVII, X = OAc). Subsequently a zinc atom transfers two electrons to this cation. The resulting carbanion (LXXXIX) is stabilised by the elimination of an acetate ion with formation of the glycal (LXXXVIII, X = H):



(LXXXVI) X = OAc (LXXXVII) (LXXXIX) (LXXXVIII).

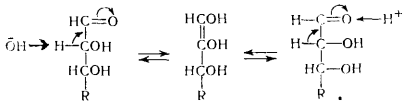
The 2-bromoglycal (LXXXVIII, X = Br) can be subjected[87] to a repeated elimination reaction by treatment with an excess of butyl-lithium. This results in the formation D-*lyxo*-hex-5-yno-1,2,3,4-tetritol (XC). The reaction constitutes a new method of synthesising carbohydrates with triple bonds:



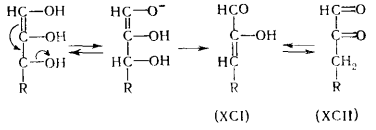
(XC).

b. β-Elimination

Many important unsaturated carbohydrates can be obtained as the result of 1,3-elimination reactions characteristic of all β-hydroxyaldehydes and β-hydroxyketones. These reactions, frequently referred to as β-elimination, are catalysed by both acids and bases. Their first stage is 1,2-enolisation, which accounts for the acid–base type of catalysis of these processes:

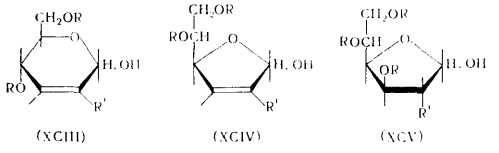


Next follows the elimination of the hydroxyl at $C_{(3)}$ with formation of the enol (XCI) which is in tautomeric equilibrium with the 3-deoxy-2-ketoglycose (XCII):



(XCI) (XCII)

The enol (XCI) can be isolated on a preparative scale only in the presence of a substituent at $C_{(2)}$, which prevents the conversion of (XCI) into (XCII). For example, in the presence of calcium hydroxide 2-*O*-methyl-D-glucose gave a high yield[88,89] of the 2-*O*-methyl ether of the enol, which exists, according to NMR spectroscopic data, as a mixture of the pyranose (XCIIIa) and furanose (XCIVa) forms, with the latter predominating:



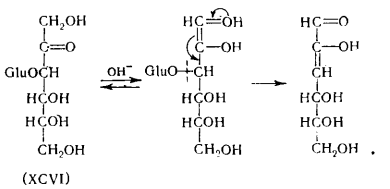
(XCIII) (XCIV) (XCV)

(a) R = H, R' = OMe; (b) R = Me, R' = OMe
(c) R = Ac, R' = NHAc

(a) R = Me, R' = OMe
(b) R = Ac, R' = NHAc.

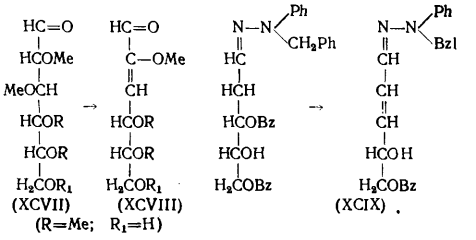
Under the influence of lime water, 2,3,5,6-tetra-*O*-methyl-D-glucose (XCVa) is rapidly converted[90,91] into the unsaturated derivative (XCIVb). On treatment with alkalies, the glucosamine derivative (XCVb) yields[92] the enamine (XCIVc).

The rate of β-elimination is determined by many factors. Thus, 2,3-di-*O*-methylglucose is converted into the enol much faster than 2-*O*-methylglucose. Hence, in order to accelerate β-elimination, it is necessary to have a substituent at the third carbon atom. Disaccharides, particularly 3-*O*-substituted derivatives, exhibit a similar behaviour. For example, 3-*O*-glucopyranosyl-D-fructose (XCVI) undergoes β-elimination in the presence of calcium hydroxide 23 times faster than D-fructose[93,94]. This also accounts for the extremely high sensitivity of such disaccharides to alkaline hydrolysis:



(XCVI)

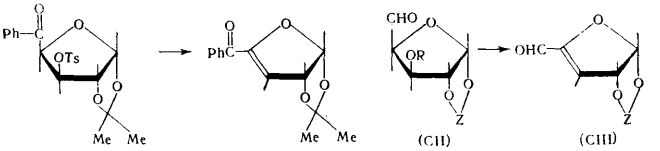
One of the factors controlling the rate of β-elimination is probably the concentration of the acyclic carbonyl form of the sugar, since this species is in fact involved in the enolisation reaction. Numerous experimental data confirming this hypothesis are now available. For example, 2,3,4,5-tetra-*O*-methylglucose (XCVII), which is distinguished by an enhanced content of the acyclic carbonyl form owing to the instability of the septanose ring, is very labile in alkalies. According to Anet's data[95], it is fully converted into the enol (XCVIII) after 2 min:



(XCVII) (XCVIII) (XCIX)
(R=Me; R_1=H)

2-Deoxy-sugars and pentoses, in which the content of the aldehydo-form is higher than in hexoses, show a very high tendency[93] to undergo β-elimination. This explains the formation of unsaturated hydrazones of type (XCIX) when attempts are made to prepare the hydrazones of 2-deoxy-sugars.

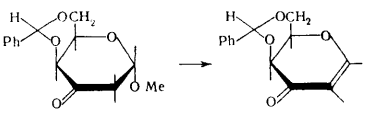
Naturally, fixed acyclic forms of hydrocarbons (the aldehydo-forms) undergo β-elimination most readily, which is sometimes employed for preparative purposes. For example, Anet[9] obtained the derivative (XCVIII, R = R_1 = Me) from the methylated aldehydo-form of glucose (XCVII, R = R_1 = Me) and Inch and Rich[96] synthesised the unsaturated ketone (CI) by heating the ketoaldose (C) with sodium carbonate in DMF. It was also shown that the dialdose derivative (CII) undergoes a similar reaction in the presence of alkalies with formation[97] of an αβ-unsaturated aldehyde (CIII):



(C) (CI) (CII) (CIII)

(R = Ts, Bzl; Z = CMe_2, C_6H_{10}).

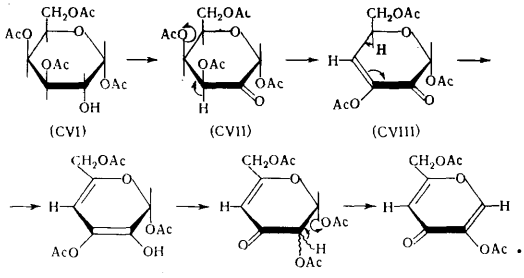
The group removed in the β-elimination reaction can also be the hydroxymethyl group at the glycosidic centre. Thus, in the presence of acids, the aldoketose (CIV) has been converted[98] into the derivative (CV):



(CIV) (CV)

Double β-elimination is possible in some cases. In particular, in the oxidation of the tetra-acetate (CVI) with DMSO in acetic anhydride in order to obtain the ketose (CVII), the diacetate of kojic acid (CXI) was obtained[99] in 84% yield. This unexpected result can be explained as follows. The ketone (CVII) formed initially undergoes β-elimination, yielding the acetate of the ketoenol (CVIII). The latter enolises further with formation of the acetate (CIX) in which the acetyl group undergoes intramolecular migration from $C_{(3)}$ to $C_{(2)}$. This results in the formation of the isomer (CX), which yields (CXI) after repeated

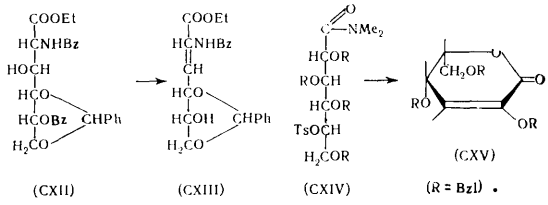
β-elimination. Since kojic acid does not contain an asymmetric carbon atom, any monosaccharide can be used to prepare it in this way:



(CVI) (CVII) (CVIII)

(CIX) (CX) (CXI)

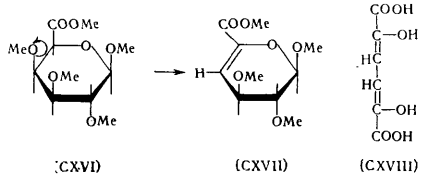
Apart from unsaturated aldoses and ketoses, unsaturated uronic, aldonic, and glycaric acid can be synthesised by the β-elimination reaction. The process proceeds via a mechanism analogous to that described above but is catalysed as a rule by bases (pyridine, sodium methoxide) or acetic anhydride. Thus methanesulphonation of ethyl 2-benzamido-4,6-*O*-benzylidene-5-*O*-benzoyl-2-deoxy-D-gluconate (CXII) led to the isolation of the unsaturated ether[1] (CXIII) instead of the expected 3-*O*-methyl derivative[1]:



(CXII) (CXIII) (CXIV) (CXV) (R = Bzl).

Treatment of the amide (CXIV) with potassium acetate in DMF gave[100] the product (CXV), which has the structure of an αβ-unsaturated lactone. A multistage mechanism has been proposed for this unusual reaction, but it requires further evidence.

It was shown above (see p. 483) that the hydrogen atom at $C_{(4)}$ in furanoses of types (C) and (CII) is acidic owing to the adjoining ring oxygen atom and an electron-accepting group. It is therefore not surprising that uronic acids can also undergo β-elimination in the presence of bases. Best results were obtained[101-103] by treating 2,3,4-tri-*O*-methyl derivatives of type (CXVI) with sodium methoxide in methanol:

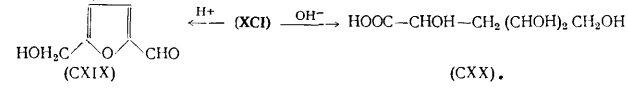


(CXVI) (CXVII) (CXVIII).

4,5-Unsaturated uronic acids of type (CXVII) have been isolated[104] following the enzymatic degradation of mucopolysaccharides. This is why conditions governing the synthesis of these interesting derivatives and the various related carbohydrates have been so carefully ascertained.

Naturally, in the deacetylation of the acetates of glycaric acids with alcoholic alkali[14], double β-elimination takes place with formation of a dienol (CXVIII).

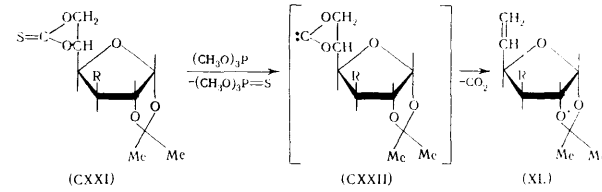
Thus a tendency towards β-elimination is characteristic of a wide variety of carbohydrates. Although frequently undesirable, this property of many sugars can be used for the preparative synthesis of unsaturated carbohydrates. However, the importance of β-elimination is not restricted to this factor. The concept of β-eliminations plays an important role in the explanations of processes such as acid and alkaline degradations of carbohydrates, which are at first sight different. As stated above (p. 483), in both cases the initial intermediate is the enol (XCI), subsequently converted either into furfural (CXIX) (or its derivatives) (acid medium) or into a glycaric acid (CXX) (alkaline medium):



(CXIX) (CXX).

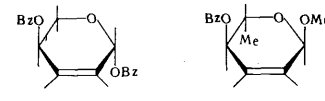
c. Elimination via the Carbene Mechanism

Among the wide variety of methods for synthesising unsaturated sugars, the formation of a double bond on stabilisation of various carbohydrate carbenes plays an important role. Sugar thiocarbonates can serve as a source of carbenes. According to the data of Horton and Turner[105,106], desulphuration of the thiocarbonate (CXXI) takes place under the influence of trimethyl phosphite. The resulting carbene (CXXII) is then stabilised by the elimination of carbonic acid, which yields 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose (XL, R = OH):



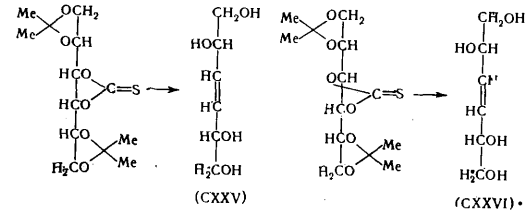
(CXXI) (CXXII) (XL)

Methyl 4,6-*O*-benzylidene-α-D-*threo*-hex-2-enopyranoside (XVI),[36] benzyl 4-*O*-benzyl-β-L-*glycero*-pent-2-enopyranoside (CXXIII), methyl 4-*O*-benzyl-6-deoxy-α-L-*threo*-hex-2-enopyranoside (CXXIV),[107] and even the Δ²,³-unsaturated nucleoside (XLII, R = Tr)[108] have been obtained similarly:



(CXXIII) (CXXIV).

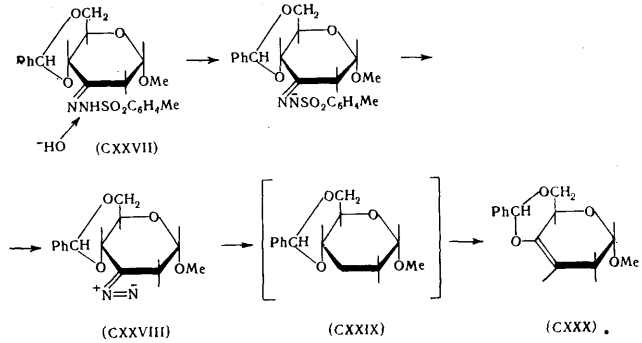
Haines[109] employed successfully the thionocarbonate method for the synthesis of the *cis*- and *trans*-isomers of 3,4-dideoxy-3,4-didehydro-D-*threo*-hexitol [compounds (CXXV) and (CXXVI)] which were isolated in the hydrolysis of substances characteristic of the blood groups:



(CXXV) (CXXVI).

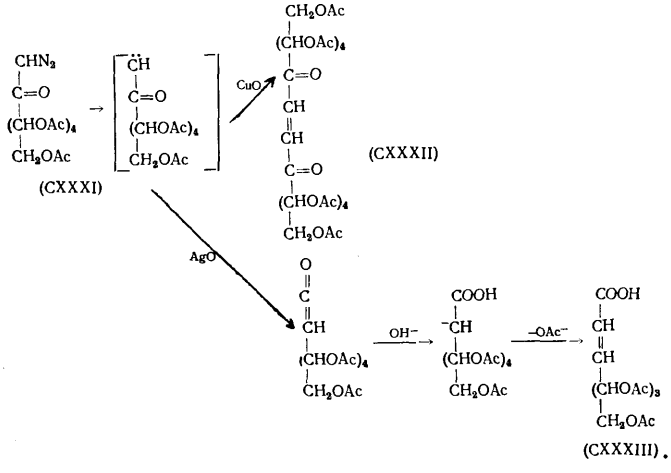
The thionocarbonate method is not the only example of the employment of carbenes for the conversion of carbohydrates into olefins. Ferrier[52] proposed a synthesis of unsaturated sugars based on the capacity of carbohydrates tosylhydrazones to yield olefins in the elimination reaction

catalysed by alkalies (the Wolff—Kishner reaction). The olefin (CXXX) was obtained in this way from the hydrazone (CXXVII). The mechanism of this elimination consists in the initial abstraction of a proton by the alkali and conversion into the diazo-compound (CXXVIII), which decomposes to the olefin (CXXX) via the intermediate carbene (CXXIX):



(CXXVII) (CXXVIII) (CXXIX) (CXXX).

The intermediate formation of a carbene has been observed[110] also in the decomposition of the acetates of 1-diazo-1-deoxyketoses (CXXXI) in the presence of copper(II) oxide, as shown by the isolation of the product (CXXXII). The decomposition of these diazoketoses in the presence of silver oxide (the Wolff rearrangement) yields[111] unsaturated acids (CXXXIII) via the mechanism



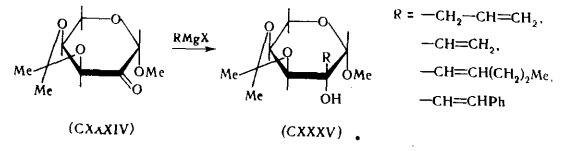
(CXXXI) (CXXXII) (CXXXIII).

2. NUCLEOPHILIC ADDITION VIA THE CARBONYL GROUP

The addition of nucleophilic agents via the carbonyl group of carbohydrates supplements significantly the methods described above for the conversion of sugars into olefins, since, apart from the introduction of a double bond, it involves an increase in the length of the carbon chain of the carbohydrate.

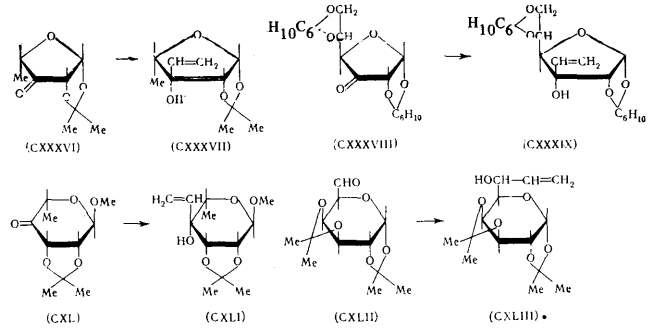
a. Interaction with Unsaturated Grignard Reagents

The condensation of the carbonyl forms of sugars with unsaturated Grignard reagents is as a rule stereospecific and therefore is frequently employed in the syntheses of carbohydrate derivatives; the method is applicable to the synthesis of streptose, 2-deoxyribose, and L-hamamelose. In their studies designed to develop the synthesis of L-hamamelose, Burton et al.[112] obtained a series of unsaturated sugar derivatives of type (CXXXV) by the condensation of methyl 3,4-*O*-isopropylidine-β-D-*erythro*-pentulopyranoside (CXXXIV) with unsaturated Grignard reagents. The preferential formation of isomers with the D-configuration at $C_{(2)}$ can be explained by the fact that the carbonyl group is screened below by the methoxy-group. Therefore only axial attack on the keto-group by the Grignard reagent is possible:



(CXXXIV) (CXXXV).

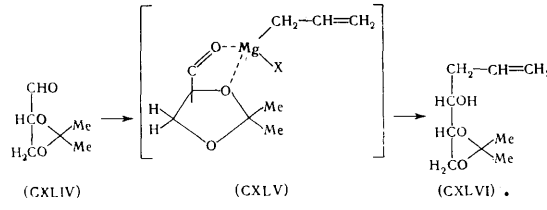
Unsaturated sugars of type (CXXXVII), (CXXXIX), and (CXLI) have been obtained by a similar procedure from the aldoketoses (CXXXVI), (CXXXVIII), and (CXL) respectively[113–115]:



(CXXXVI) (CXXXVII) (CXXXVIII) (CXXXIX)

(CXL) (CXLI) (CXLII) (CXLIII).

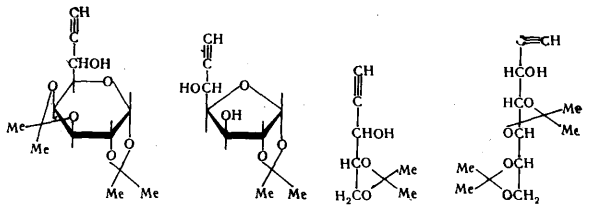
Apart from ketones, the aldehydo-forms of carbohydrates have been used for condensation with unsaturated organometallic compounds. The condensation of vinylmagnesium bromide and the dialdose (CXLII) yields[64,116] a mixture of isomeric unsaturated carbohydrates in which compound (CXLIII) predominates. Hough[3] obtained 1,2-*O*-isopropylidinehex-5-ene-1,2,3-triol (CXLVI) from isopropylidene-D-glyceraldehyde (CXLIV) and allylmagnesium bromide. The preferential formation of the isomer with the D-*ribo*-configuration becomes understandable if one postulates the existence of an intermediate magnesium complex (CXLV), proposed earlier[117,118] to account for similar reactions:



(CXLIV) (CXLV) (CXLVI).

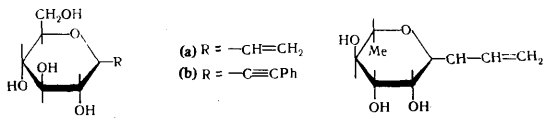
So far the Grignard reaction is the only general method for the introduction of a triple bond into the carbohydrate molecule. Thus the interaction of various aldehydo-forms of sugars with ethynylmagnesium bromide yielded[119–123] a

series of ethynyl derivatives of carbohydrates of the type (CXLVII)—(CL):



(CXLVII) (CXLVIII) (CXLIX) (CL)

It is interesting to note the preferential formation of the product (CXLVIII) with the D-configuration at $C_{(5)}$, which can also be accounted for by the formation of a magnesium complex analogous to (CXLV). The interaction of acetohalogenoses with unsaturated organomagnesium compounds constitutes a remarkable complication of the Grignard reaction in carbohydrate chemistry. Compounds (CLI, a and b) and compound (CLII) were obtained respectively from acetobromoglucose[124,125] and acetobromorhamnose[126]:

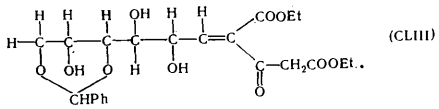


(a) R = —CH=CH$_2$
(b) R = —C≡CPh

(CLI, a and b) (CLII)

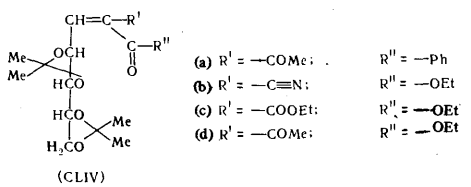
b. The Knoevenagel—Döebner Condensation

The reactivity of the carbonyl forms of sugar have also been used to synthesise unsaturated carbohydrates by the Knoevenagel—Döebner reaction. The interaction of 4,6-*O*-benzylidene-D-glucose with acetonedicarboxylic acid ester in the presence of piperidine yielded[127,128] the unsaturated ketoacid (CLIII):



(CLIII)

Zimmer et al.[129] investigated the reaction of a series of compounds with an active methylene group (benzoylacetone and malonic, cyanoacetic, and acetoacetic esters) with the al-form of 2,3:4,5-di-*O*-isopropylidene-D-arabinose. They isolated the unsaturated branched-chain sugars (CLIV, a—d):



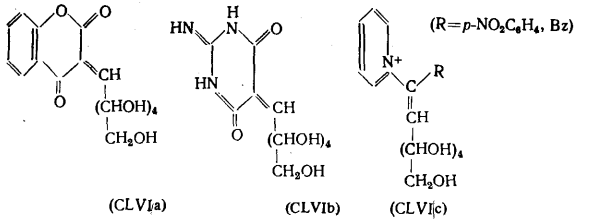
(a) R' = —COMe; R'' = —Ph
(b) R' = —C≡N; R'' = —OEt
(c) R' = —COOEt; R'' = —OEt
(d) R' = —COMe; R'' = —OEt

(CLIV)

When malonic acid was employed, unsaturated acids of type (CLV) were obtained similarly[130,131]:

R—CH=CHCOOH (CLV) (R = sugar residue).

A whole series of unsaturated sugars with heterocyclic groups (CLVI, a—c) have been synthesised by condensing the acetates of the aldehydo-forms of hexoses with the active methylene groups of 5-hydroxycoumarin[132], iminobarbituric acid[133,134], and Kröhnke [sic] salts[135]:

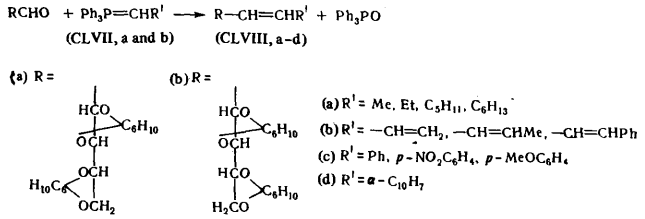


(CLVIa) (CLVIb) (CLVIc)

C-glycosylated 4-hydroxycoumarins (CLVIa) exhibit a high anticoagulant activity, surpassing somewhat heparin in the duration of its activity.

c. The Wittig Reaction

Among other condensation methods for synthesising unsaturated hydrocarbons, the most elegant and modern techniques involve the interaction of phosphoranes with the carbonyl forms of sugars (the Wittig reaction)[136]. The process is interesting because it is universal, takes place under mild conditions, and makes it possible to introduce a double bond into the monosaccharide molecules in a specific position. Intense studies on the conversion of carbohydrates into olefins by the Wittig reaction[137] showed the possibility of the synthesis of a wide variety of unsaturated sugar derivatives—*C*-glycosylated derivatives of aliphatic, aromatic, and heterocyclic compounds, and unsaturated aldoses, ketoses, and aldonic acids. Cyclic and acyclic aldehydo-forms of carbohydrates are usually employed as the carbonyl component. Free monosaccharides are inconvenient, since the products with a polyol residue obtained from them are unstable under the conditions of the Wittig reaction (p. 490). The choice of the aldehydo-form in each specific case depends on the reaction conditions and the reactivity of the phosphorane employed. For example, only the aldehydo-forms with acetal, methyl, and benzyl protecting groups can be employed for condensation[138] with reactive group I phosphoranes, since with acetylated aldehydo-forms of the sugars the phosphoranes are involved in side reactions with the protecting groups. In particular, condensation of 2,3:4,5-di-*O*-cyclohexylidene derivatives of the aldehydo-forms of L-arabinose and D-xylose with a wide variety of group I phosphoranes enabled Zhdanov and coworkers[139-144] to synthesise a series of unsaturated polyols with the general formula (CLVIII, a—d). Depending on the structure of the group R', the products obtained can be assigned to various classes of organic compounds: *C*-glycosylated ethylenes (CLVIIIa), butadienes (CLVIIIb), styrenes (CLVIIIc), and vinylnaphthalenes (CLVIIId):



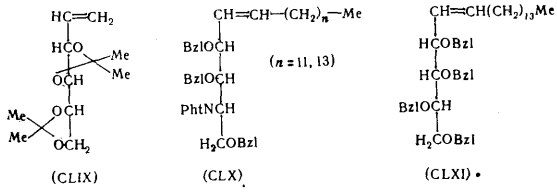
RCHO + Ph$_3$P=CHR' → R—CH=CHR' + Ph$_3$PO
(CLVII, a and b) (CLVIII, a-d)

(a) R = (b) R =

(a) R' = Me, Et, C_5H_{11}, C_6H_{13}
(b) R' = —CH=CH$_2$, —CH=CHMe, —CH=CHPh
(c) R' = Ph, *p*-NO$_2$C$_6$H$_4$, *p*-MeOC$_6$H$_4$
(d) R' = α-C$_{10}$H$_7$

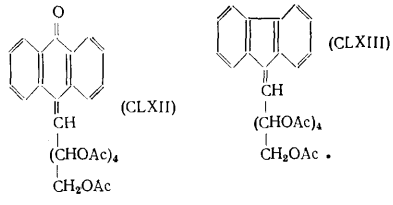
Tronchet et al.[145] synthesised similarly 1,2:3,4-di-*O*-isopropylidene-$C_{(1)}$-vinyl-L-*arabino*-tetritol (CLIX). The condensation of the aldehydo-forms of 2,3,5-tri-*O*-benzyl-4-phthalimido-L-ribose and of

2,3,4,5-tetra-*O*-benzyl-L-lyxose with triphenyl-, n-tridecylidene-, or n-pentadecylidene-phosphoranes yielded[146,147] unsaturated derivatives of the polyols (CLX) and (CLXI) used subsequently in the syntheses of phytosphingosines:



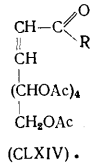
(CLIX) (CLX) (CLXI).

C-Substituted unsaturated polyols can be synthesised also with the aid of certain relatively inactive group III phosphoranes. In this case one can employ the aldehydo-forms of carbohydrate acetates; thus compound (CLXII), similar in structure to natural aloins, was obtained in this way from 10-anthronylidenetriphenylphosphorane and the penta-acetate of the aldehydo-form of D-galactose[148]. A fluorene derivative (CLXIII) was synthesised by a similar procedure[148]:



(CLXII) (CLXIII)

The Wittig reaction is particularly valuable as a method for the introduction into the carbohydrate molecule of active functional groups together with the double bond. One employs for this purpose phosphoranes of the second kind which are stable under the usual conditions and are fairly reactive. Thus the Wittig reaction has proved convenient for the synthesis of higher unsaturated $C_{(1)}$-substituted ketoses. According to the data of Zhdanov and coworkers[149-152], the interaction of the acetates of the aldehydo-forms of hexoses with acetyl-, aroyl-, and acyl (from heterocyclic acids) derivatives of methylene phosphoranes constitutes a preparative synthesis of these interesting carbohydrate derivatives having the general formula (CLXIV):



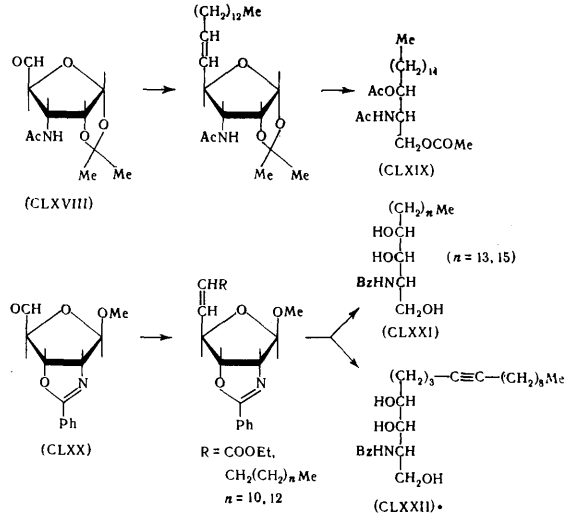
R=Me, Ph—NO_2-*p*, Ph—Br-*p*, Ph—(OMe)-*p*, $C_6H_2(OMe)_3$, $C_6H_3(OMe)_2$, α-thienyl or fury

(CLXIV).

The condensation of formylmethylenetriphenylphosphorane with the aldehydo-forms of (CII) and (CLVII) can serve as a general method of synthesising[142,153] unsaturated aldoses of type (CLXIV), which are difficult to obtain:

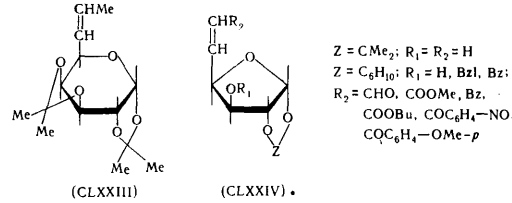
RCH=CH—CHO (CLXV) (R = carbohydrate residue)

The use of partly protected dialdoses and their derivatives greatly extends the scope of the Wittig reaction in the series of carbohydrates. One then introduces into the condensation with phosphoranes only one aldehyde group, while the second, which is temporarily protected, can be subsequently used for further reactions. The sphinogisines (CLXIX), (CLXXI), and (CLXXII) were synthesised in this way from the corresponding dialdoses (CLXVIII) and (CLXX):



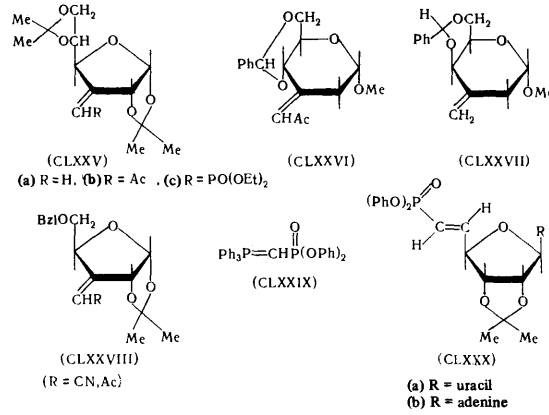
(CLXVIII) (CLXIX) (CLXX) (CLXXI) (CLXXII).

A series of unsaturated aldoses of types (CLXXIII) and (CLXXIV) were obtained also from dialdoses of a similar structure[150,157-159]:



(CLXXIII) (CLXXIV).

Branched-chain sugars (CLXXV)—(CLXXVIII), which are difficult to obtain, have been synthesised from ketoaldoses by the Wittig reaction[157,160-164]:



(CLXXV) (CLXXVI) (CLXXVII)

(a) R=H, (b) R = Ac, (c) R = PO(OEt)$_2$

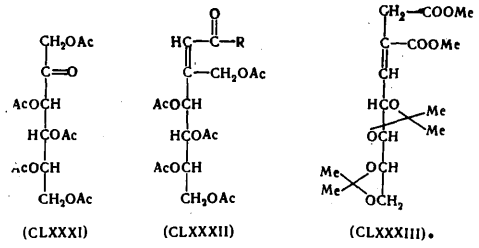
(CLXXVIII) (CLXXIX) (CLXXX)

(R = CN, Ac) (a) R = uracil (b) R = adenine

The branched-chain monosaccharides with a C—P bond (CLXXV), synthesised[165] from 1,2:5,6-di-*O*-isopropylidene-D-*ribo*-3-hexulofuranose and tetraethyl methylenediphosphonate are of considerable interest. The unsaturated carbohydrate phosphonate (CLXXV) was used further to synthesise modified nucleotides. Jones and Moffatt[166] showed that the condensation of phosphonylmethylenephosphorane (CLXXIX) with $C_{(4)}$-formyl-2,3,-*O*-isopropylidene-derivatives of uridine and adenosine yields 5′-deoxy-5′-(*OO*-diphenylphosphonomethylene)uridine (CLXXXa) and the analogous adenosine derivative

(CLXXXb). Similar condensations lead to convenient pathways to the synthesis of modified nucleotides.

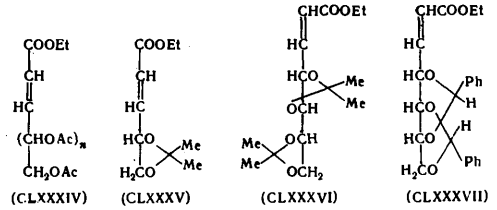
On treatment with an acylmethylenephosphorane, the penta-acetate of the keto-form of L-sorbose (CLXXXI) also yields[167] a sugar with an olefinic bond (CLXXXII):



(CLXXXI) (CLXXXII) (CLXXXIII).

The methyl ester of 3,4-dehydro-2,3,4-trideoxy-5,6:7,8-di-*O*-isopropylidene-3-methoxycarbonyl-L-*arabino*-octonic acid (CLXXXIII) was obtained by a similar procedure from phosphoranes with an iso-structure and the aldehydo-form of 2,3:4,5-di-*O*-isopropylidene-L-arabinose[167].

The bulk of the studies on the Wittig reaction in carbohydrate chemistry concern the synthesis of $\alpha\beta$-unsaturated acid esters. Kochetkov and Dmitriev[168] developed on the basis of these compounds a new and convenient method of synthesising higher sugars. Starting with a wide variety of aldehydo-forms of carbohydrates and alkoxycarbonylmethylenetriphenylphosphoranes, they obtained[169-175] a series of esters of *trans*-2,3-didehydro-2,3-dideoxyaldonic acids of types (CLXXXIV, a and b)—(CLXXXVII):

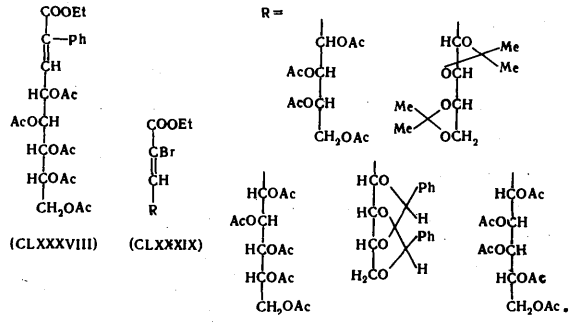


(CLXXXIV) (CLXXXV) (CLXXXVI) (CLXXXVII)

(a) $n = 3$, L-*arabino*-, D-*arabino*-

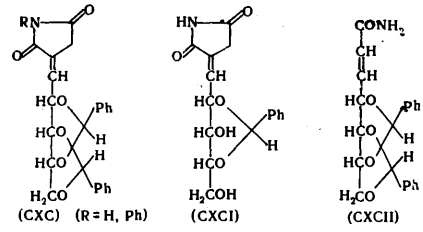
(b) $n = 4$, D-*gluco*-, D-*galacto*-

The employment of modified alkoxycarbonylmethylenetriphenylphosphoranes makes it possible to obtain[176,177] interesting derivatives of $\alpha\beta$-unsaturated acids (CLXXXVIII) and (CLXXXIX). The latter were used by Kochetkov and Dmitriev[177] to synthesise aziridine derivatives of carbohydrates:

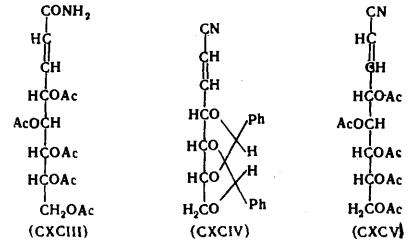


(CLXXXVIII) (CLXXXIX)

A series of unsaturated carbohydrates (CXC)—(CXCV) have been obtained from phosphoranes with maleimide, amide, and nitrile substituents[175,178]. The derivatives (CXC) and (CXCI) were synthesised for further use in the synthesis of the antibiotic Showdomycin[175]:

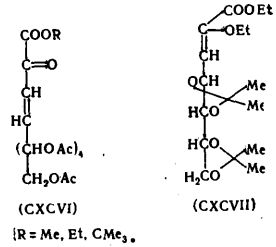


(CXC) (R = H, Ph) (CXCI) (CXCII)



(CXCIII) (CXCIV) (CXCV)

Interesting pathways to the synthesis of 3-deoxy-2-oxoaldonic acids and their amino-derivatives (sialic acids), which are widely distributed[3] in nature, have been outlined on the basis of the Wittig reaction. These acids are formed in the organism by the condensation of monosaccharides with phosphoenolpyruvic acid. Therefore it was natural to investigate the interaction of the aldehydo-forms of carbohydrates with alkoxycarbonyloxomethylenephosphoranes obtained from bromopyruvic acid esters. This led to the synthesis[179,180] of unsaturated ketoacids of the general formula (CXCVI). Further reactions of these products, investigated by Kochetkov and coworkers[181-183], led to the synthesis of 2-deoxy-3-oxoaldonic acids identical with the natural products:

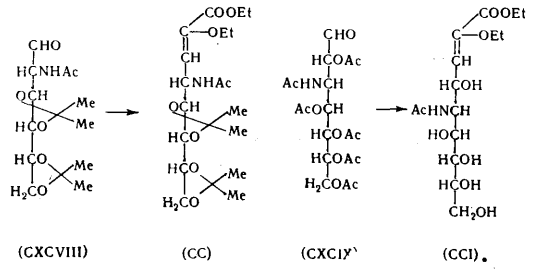


(CXCVI) (CXCVII)

(R = Me, Et, CMe_3).

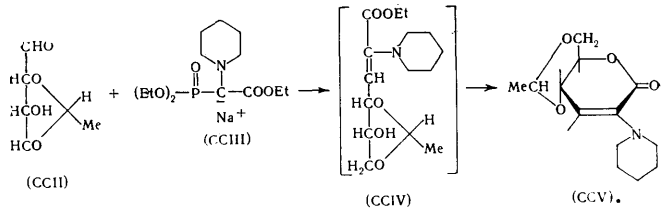
Samokhvalov and coworkers[184] obtained the fixed enolic forms (CXCVII) of an α-ketoacid from the aldehydo-forms of 2,3:4,5-di-*O*-isopropylidene-D-arabinose and ethoxycarbonylethoxymethylenetriphenylphosphorane. They demonstrated that the product (CXCVII) is also convenient for the synthesis of 2-deoxy-3-oxoaldonic acids. The use of derivatives of the aldehydo-forms of glucosamine (CXCVIII) and heptosamine (CXCIX) [185,186] for condensation with ethoxycarbonylethoxymethylenetriphenylphosphorane permits the synthesis of the starting materials (CC) and

(CCI) for the preparation of neuraminic acid and its analogues:



(CXCVIII) (CC) (CXCIX) (CCI).

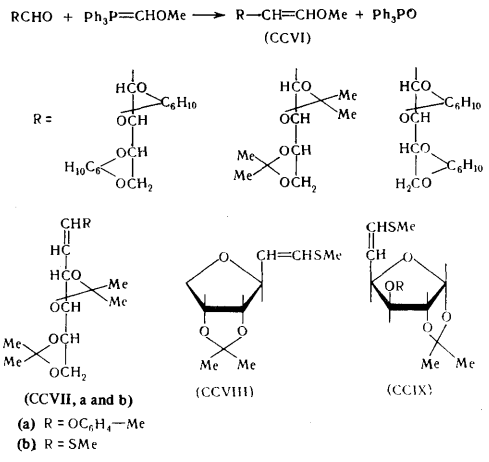
The simplest and novel synthesis of 3-deoxy-2-octoaldonic acids was proposed by Baschang and Tritz[187], who employed for this purpose the condensation of the sodium salt of ethyl *OO*-diethylphosphonopiperidinoacetate (CCIII) with 2,4-*O*-ethylidene-D-erythrose (CCII). They obtained as a result the enaminolactone (CCV) without isolating the intermediate enaminoester (CCIV):



(CCII) (CCIII) (CCIV) (CCV).

The enaminolactone (CCV) can be subsequently converted under mild conditions into the corresponding 3-deoxy-2-oxoaldonic acid. Further development of this reaction may lead to the elaboration of a convenient method of synthesising 3-deoxyhexulonic acids, including sialic acids.

The vinyl ethers employed in the syntheses of 2-deoxyaldoses are also unsaturated carbohydrate derivatives obtained by the Wittig reaction. The condensation of derivatives of the aldehydo-forms with methoxymethylenetriphenylphosphorane yielded[141,145,188-190] the vinyl ethers (CCVI) and the interaction of the aldehydo-form of 2,3:4,5-di-*O*-isopropylidene-L-arabinose with methylenetriphenyltolyloxyphosphorane gives[191] aromatic vinyl ethers of type (CCVIIa):

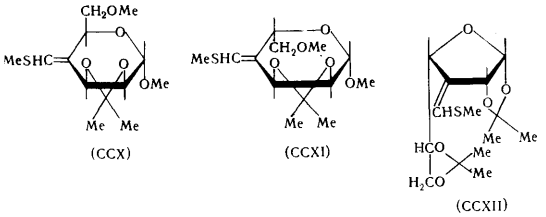


(CCVII, a and b)
(a) R = OC_6H_4—Me
(b) R = SMe

(CCVIII) (CCIX)

In the search for other precursors of 2-deoxy-sugars, attention was turned to methylenemethylthiotriphenylphosphorane, which was employed by Tronchet and coworkers[190,192] for condensation with various aldehydo-forms. The methylthio-derivative (CCVIIb) was prepared in this way[190] from the aldehydo-form of 2,3:4,5-di-*O*-isopropylidene-L-arabinose. A similar treatment of 2,5-anhydro-3,4-*O*-isopropylidene-D-ribose and 1,2-*O*-isopropylidene-3-*O*-methyl-(and 3-*O*-benzyl-)-α-D-*xylo*-pentodialdo-1,4-furanoses led[192] to the synthesis of the corresponding vinyl thioethers (CCVIII) and (CCIX).

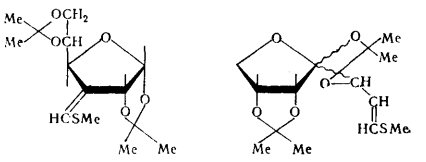
The interaction of methylenemethylthiotriphenylphosphorane with certain protected keto-sugars proved to be more complex. Thus 2,3-*O*-isopropylidene-6-*O*-methyl-α-D-*lyxo*-3-hexulopyranoside gives the vinyl thioethers[193] (CCX) and (CCXI) in a yield of only 20%:



(CCX) (CCXI) (CCXII)

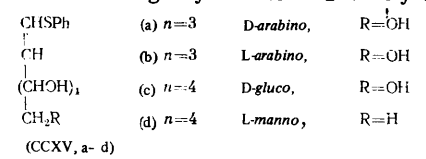
The formation of the side product (CCXI) is probably a result of the epimerisation of a similar ketose at $C_{(5)}$ in the course of enolisation induced by the basic medium.

It is interesting that epimerisation is not observed with 1,2:5,6-di-*O*-isopropylidene-α-D-*xylo*-3-hexulofuranose, since only the normal reaction product (CCXII) has been isolated[194]. The same reaction with 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-3-hexulofuranose proved to be much more complicated[195,196], since, apart from the expected vinyl thioester (CCXIII), the $C_{(5)}$ epimer (CCXII) was isolated as well as the unexpected rearrangement product (CCXIV):



(CCXIII) (CCXIV)

Apart from methylenemethylthiotriphenylphosphorane, methylenephenylthiotriphenylphosphorane can be used to synthesise vinyl thioethers. Thus, according to the data of Bestmann and Angerer[197], this phosphorane reacts smoothly even with the free sugars in DMSO, forming the corresponding aryl vinyl thiovinyl ethers (CCXV, a—d). Since the products (CCXVa) and (CCXVb) were converted further into 2-deoxy-D-(and L-)-*arabino*-hexoses, it is a very convenient two-stage synthesis of 2-deoxy-sugars:



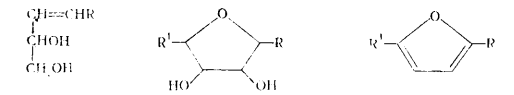
(CCXV, a- d)

(a) $n=3$	D-*arabino*,	R=OH
(b) $n=3$	L-*arabino*,	R=OH
(c) $n=4$	D-*gluco*,	R=OH
(d) $n=4$	L-*manno*,	R=H

A number of studies by Kochetkov and coworkers[189,199], who made a detailed investigation of the condensation of alkoxycarbonylmethylenetriphenylphosphoranes with D-arabinose, D-ribose, D-glucose, D-galactose, D-glycero-D-*gulo*-heptose, and 2-acetamido-2-deoxy-D-glucose, were devoted to the employment of free and partially protected sugars in the Wittig reaction. They obtained the corresponding esters of *trans*-2,3-didehydro-2,3-dideoxyaldonic acids in yields of 45%. The decrease of yield is probably due to the formation of cyclic side

products. To prevent such cyclisation, partly protected sugars were employed. For example, the use of 2,3,4,6-tetra-*O*-acetyl-D-galactose instead of free D-galactose increases the yield of the required product to 80%. Similarly when 2-acetamido-2-deoxy-D-glucose is replaced by its 4,6-*O*-benzylidene derivative, the yield of the normal product of the condensation with methoxycarbonylmethylenetriphenylphosphorane increases from 30 to 50%.

The problem of the employment of free and partly protected sugars in the Wittig reaction with alkoxycarbonylmethylenetriphenylphosphoranes was investigated in greater detail by Zhdanov and coworkers[200-204], who showed that the required product is formed only with DL-glyceraldehyde (CCXVI):



(CCXVI) (CCXVII) (CCXVIII)

(R = CO Me, COPh) (R = CH_2OH, $(CHOH)CH_2OH$ (R = Me, Ar; R^1 = CH_2COAr, CH_2COMe) R^1 = $(CHOH)_n CH_2OH$)

When various pentoses and hexoses were allowed to interact with group II phosphoranes, the anhydro-derivatives were isolated, compounds of type (CCXVII) being formed preferentially. During the reaction, these anhydro-derivatives are dehydrated, probably under the influence of the excess phosphorane, with formation of substituted furans (CCXVIII). Thus the results show that conformational factors, and particularly the preference for specific conformations in the opening of the cyclic forms of aldoses at the instant of reaction, play a decisive role in the formation of a particular product.

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Rostov State University

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Methods of Synthesis of Pyrimidine Nucleosides

B.N.Stepanenko, E.M.Kaz'mina, and Z.S.Dubinkina

The review describes the present state of knowledge about the synthesis of pyrimidine nucleosides. Together with a description of various methods of synthesis, their comparative characteristics are stated briefly. The bibliography includes 188 references.

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I. INTRODUCTION

The chemistry of nucleosides and nucleic acids is at present one of the most vigorously developing fields despite the considerable difficulties facing investigators engaged in it. The interest in the chemistry of nucleosides is quite understandable. There are good grounds for attributing to the analogues of nucleosides the capacity to influence heredity, to act on the development of viruses, and to suppress the growth of malignant tumors. Finally the availability of a large set of various nucleosides constitutes an essential condition for theoretical studies on the mechanism of the biosynthesis of nucleic acids and proteins, on the specificity of the relevant enzymes, etc.

In view of the great interest in the chemistry of nucleosides, the literatures in this field is exceptionally large. The compilation of a detailed review on the chemistry of all the groups of nucleosides became difficult a long time ago [1-6]. This is undoubtedly the reason why it has already been possible for some time to publish in the periodical literature reviews dealing with a particular single group of nucleosides [1,7,8] or one of the methods of synthesis [9,10]. Thus a very good review by Fox and Wempen [1], dealing only with the methods of synthesis of pyrimidine nucleosides (and yet including 6-7 pages of references), was published in 1959 in Advances in Carbohydrate Chemistry.

During more than ten years which have elapsed since the publication of the review, a number of earlier methods of synthesis have been further improved and have been given a theoretical basis (for example the metal salts and the Hilbert-Johnson methods). The silyl modification of the Hilbert-Johnson method has been developed.

The method involving the modification of existing nucleosides has been supplemented by a number of new reactions, for example nucleosides containing the 5',6- and 2',6-anhydro-linkages [11-15], sulphur [16,17], halogens [18,19], a double bond in the sugar residue [20], etc. have been obtained.

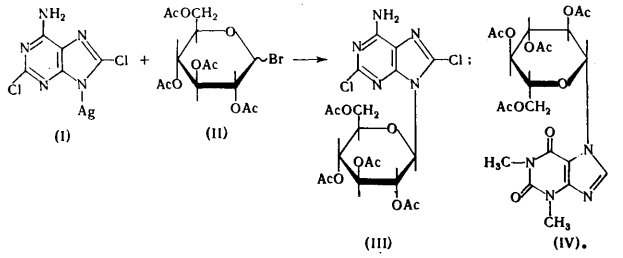
Considerable practical advances have been made in nucleoside chemistry. The possibility of clinical application of nucleosides as antiviral agents was demonstrated for the first time for the familiar thymidine analogue 2-deoxy-5-iodouridine in the treatment of herpetic affections of the eyes [21].

Data on the biological activities of a large number of synthetic nucleosides and the possibility of their clinical application can be found in a number of reviews [22-24].

The aim of the present review was to describe the present state of knowledge of the synthesis of pyrimidine nucleosides, including the literature up to the middle of 1971.

II. THE METAL SALTS METHOD

Fischer and Helferich [25] were the first to achieve the condensation of the silver salt of 2,8-dichloroadenine (I) and theophylline with 2,3,4,6-tetra-*O*-acetylglucopyranosyl bromide (II) which led to the synthesis of 2,8-dichloro-9-(2',3',4',6'-tetra-*O*-acetyl-β-D-glucopyranosyl)adenine (III) and 7-(2',3',4',6'-tetra-*O*-acetyl-β-D-glucopyranosyl)-theophylline (IV) respectively:



(I) (II) (III) (IV).

After deactylation and dehalogenation of compound III, 9-(β-D-glucopyranosyl) adenine, the first synthetic nucleoside, was obtained.

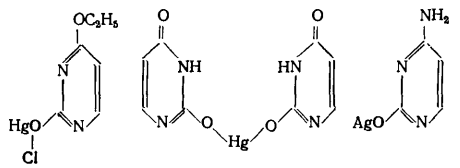
However, it was found that the silver salts of purines and pyrimidines containing the tautomeric group $-\overset{|}{N}-\overset{\|}{C}- \rightleftharpoons -N=\overset{|}{C}-$ (H, O, OH), such as uracil, cytosine, and theobromine, react with acetohalogeno-sugars to form products which reduce Fehling's reagent and are labile in relation to acids and alkalis. Fischer [26] suggested that these derivatives are probably *O*-glycosides.

Levene and Sobotka [27] reached the same conclusion on the basis of experiments in which the silver and potassium salts of cytosine and certain substituted uracils were condensed with glycosyl halides to form unstable products.

For this reason, the reaction of metals salts of pyrimidines with glycosyl halides was not investigated until the successful synthesis of nucleosides using mercury salts of purines [28] led to the investigation of the analogous pyrimidine derivatives and it was found [29,30] that

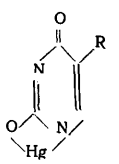
N-glycosides can be obtained from them in satisfactory yields; for example, thyminyl riboside and thyminyl xyloside were synthesised from dithyminylmercury and cytidine was obtained from *N*-acetylcytosinylmercury. It was noted that the reactions of certain mercury salts with deoxyribosyl halides take place with formation of *O*-deoxyribosides and not *N*-deoxyribosides [31]. In order to obtain *N*-deoxyribosides, it is necessary to employ the mercury salts of pyrimidine containing the pyrimidine base and mercury in proportions of 1 : 1. [32,33]

A number of hypotheses have been put forward to account for these results and the finding that the silver and mercury salts yield different products [34-36]. It was suggested that the chloromercury salt (V) of a pyrimidine, the dipyrimidine mercury compound (VI), and the silver salt (VII) of a pyrimidine are oxygen derivatives which react with glycosyl halides with the initial formation of *O*-glycosides, most of which rearrange to *N*-glycosides under the reaction conditions:



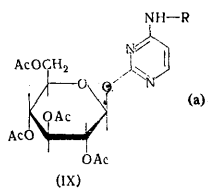
(V) (VI) (VII).

Since in monopyrimidine compounds of mercury, the heavy metal is probably also linked to the nitrogen atom, as in compound (VIII), these substances yield *N*-glycosides directly [37]:



(VIII) (R=H,CH$_3$, F, Br, I).

Fischer's method [26] (the preparation of the silver salt of cytosine and its condensation with acetobromoglucose in boiling xylene) was modified [38] but, as in Fischer's original work, the final product was an *O*-glycoside (IXa): [39]

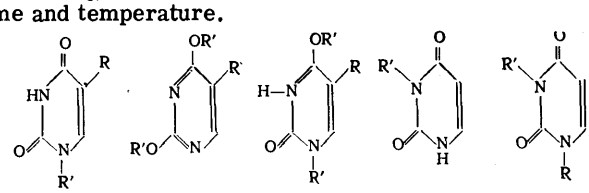


(a) R = H; (b) R = CH$_3$CO.

(IX)

On heating with mercury(II) bromide in xylene, the acetylated nucleoside (IXa) isomerises to an *N*-nucleoside with a very low yield. The best result was obtained in the condensation of the silver salts of *N*-acetylcytosine with acetobromoglucose in boiling xylene, compound (IXb) being formed. The reaction of the chloromercury salt of uracil (V) with acetobromoglucose, which has been reinvestigated, is of practical interest, but Ukite et al. [40] found that Fox's method [condensation of the chloromercury salt of 4-ethoxy-2(1*H*)-pyrimidinone with acetobromoglucose in boiling xylene] is not adequately reproducible.

Interesting data were obtained in a study of the reaction of metal salts of uracil and thymine [41-43] and also of 2-thiouracil [44] with acetobromoglucose and tribenzoylribofuranosyl chloride. The reaction of the silver salt of uracil with acetobromoglucose in toluene gives a mixture of five products [(Xa), [45] (XIa), (XIIa), (XIII), and (XIV) [42,43]], the proportions of which vary with reaction time and temperature.



(X) (XI) (XII) (XIII) (XIV).

[R' = 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl; (a) R = H; (b) R = CH$_3$]

A similar reaction with thymine yields the known compounds (Xb), [29] and (XIb) [46] and compound (XIIb), which was not characterised previously.

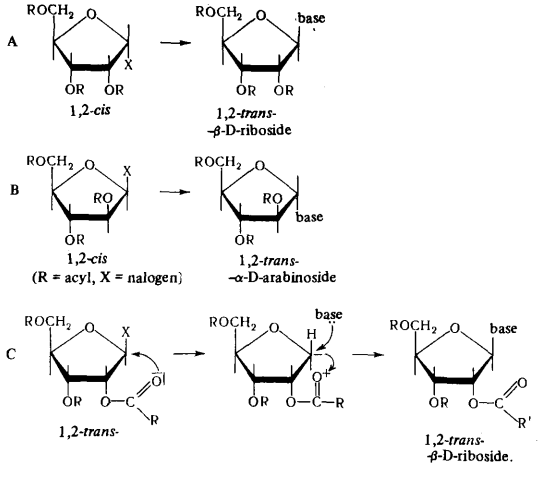
In the reaction of the silver salts of uracil and thymine with tribenzoylribofuranosyl chloride [41] in boiling xylene for 7 h, satisfactory yields of 1-(2',3',5'-tri-*O*-benzoyl-β-D-ribofuranosyl)-uracil and -thymine were obtained. Thus the views expressed in literature that the silver salts of uracil are incapable of undergoing the *N*-glycosylation reaction under the influence of acylglycosyl halides were disproved yet again [3]. The use of the mercury salt in the reaction with acylglycosyl halides leads to the formation of a more complex mixture of products and to a sharp decrease of the yield of the *N*-nucleoside [41].

A modification of the Helferich method [47-50], which was first employed by Fox and coworkers [47] to synthesise acylated pyrimidine nucleosides, is nowadays used fairly often for the synthesis of pyrimidine nucleosides. This method is suitable for the preparation of thymine and uracil derivatives without the preliminary isolation of mercury derivatives of the heterocyclic bases. Free bases are used in the synthesis but in the case of amino-derivatives it is desirable to protect the amino-group by acylation before the condensation reaction. However, it was shown recently that 2-thiocytosine [49] can be introduced into the reaction directly. Particularly high yields are obtained for pyrimidines containing electronegative groups at C$_{(5)}$.

1. Stereochemistry of the Synthesis of Nucleosides

The synthesis of nucleosides from acetobromoglucose having the α-configuration at C$_{(1)}$ leads to compounds with the β-configuration and therefore the reaction presumably involves an S$_N$2 mechanism with direct attack by the electrophilic C$_{(1)}$ atom of α-acetobromoglucose on the nucleophilic nitrogen atom of the pyrimidine or purine derivative. In the synthesis of natural β-nucleosides, syrupy ribofuranosyl halides containing a mixture of α- and β-forms are used as starting materials. In the synthesis of puromycin [51], crystalline 2,5-di-*O*-benzoyl-3-deoxy-3-phthalimido-β-D-ribofuranosyl chloride yields exclusively the β-nucleoside. To account for these observations, Baker and coworkers [52,53] suggested that, in the condensation of the purine (or pyrimidine) derivative of a heavy metal with an acetylated glycosyl halide, the product is a nucleoside with a C$_{(1)}$-C$_{(2)}$-*trans*-configuration of the sugar regardless of the initial configuration of these atoms. Usually in the reactions of halogeno-sugars with the C$_{(1)}$-C$_{(2)}$-*cis*-configuration, there is a simple Walden inversion and the resulting nucleoside has the C$_{(1)}$-C$_{(2)}$-*trans*-configuration, which can be either the α- or β-form depending on the configuration of the sugar

(mechanism A and B).[2] $C_{(1)}$ -$C_{(2)}$-*trans*-halogeno-sugars are involved in two S_N2 reactions (with a double Walden inversion); initially the configuration at $C_{(1)}$ is inverted with participation of the adjacent $C_{(2)}$-acyloxy-group and the formation of an orthoester ion and then in the reaction of the base a second inversion takes place (mechanism C).[2]



Although the reaction mechanisms are completely different for the two anomeric halides, a nucleoside with a *trans*-arrangement $C_{(1)}$ and $C_{(2)}$ is formed in both cases regardless of the configuration of the anomeric halide at $C_{(1)}$ when the halogen atom is replaced by nucleophilic groups.

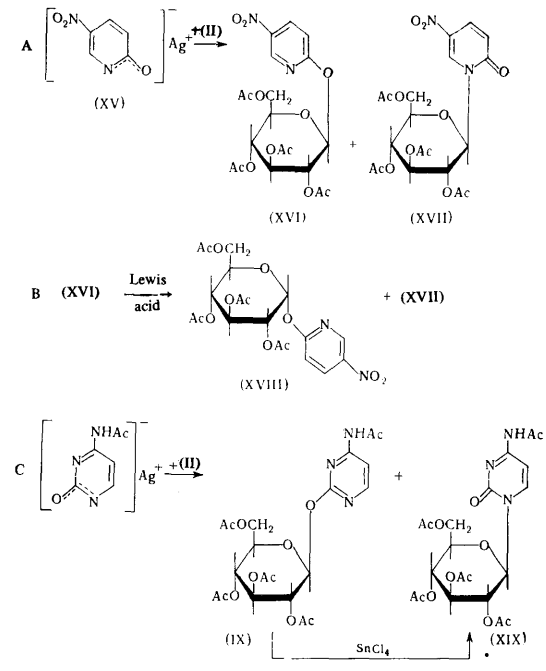
It has been shown that the rule is well founded and is actually employed at present to demonstrate a particular configuration. However, in certain cases a small amount of the other anomer is formed together with the one expected. Thus in the ribofuranosyl halide having a 2,3-cyclocarbonate protecting group and also in derivatives of 2-deoxy-D-ribose, there is no directing effect of the 2-acyloxy-group; in such cases the α- and β-forms of the nucleosides should be obtained and are in fact obtained[54,55].

2. The Mechanism of the Synthesis of Nucleosides

The mechanism of the synthesis of nucleosides and similar glycosides from glycosyl halides and metal salts of heterocyclic bases containing the $-\underset{|}{\overset{H}{N}}-\overset{\|}{\underset{O}{C}}-$ group has been investigated extensively in recent years[2,36,38,56,57,58]. It was shown in early investigations that mercury halides catalyse the O → N glycosyl rearrangement. Wagner and coworkers[59] demonstrated the possibility of such rearrangements for various heterocyclic systems.

It was observed that in certain cases heterocyclic *O*-glycosides do not rearrange to *N*-glycosides in the presence of mercury halides, products which are anomeric *O*-glycosides being obtained instead[60]. Thacker and Ulbricht reinvestigated the glycosides of 5-nitro-2-pyridone[57,58], since in Wagner's studies the aglycones (including 5-nitro-2-pyridone) were powerful electron acceptors.

The reaction of the silver salt of 5-nitro-2-pyridone (XV) with acetobromoglucose (II) is the *O*-glucoside (XVI) which was believed[60] to be the α-anomer on the basis of the method of synthesis (mechanism A). Treatment of this product with a Lewis acid (mercury bromide) in boiling xylene gives the isomeric *O*-glucoside (XVIII) which was assumed[60] to be the α-anomer (mechanism B)

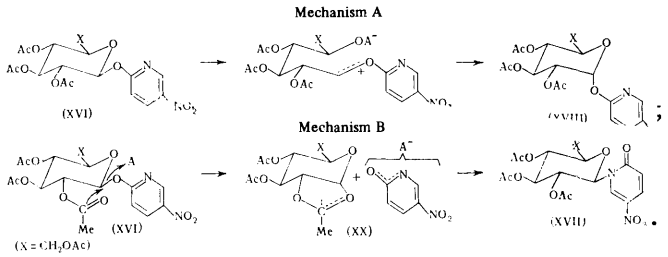


It was established by the NMR method[58] that compounds (XVI) and (XVIII) are in fact the β- and α-anomers and in addition thin-layer chromatography revealed the presence, together with compound (XVIII), of a product (XVII) which is a β-*N*-glycoside. Consequently an O → N rearrangement takes place in this case, its occurrence depending on the temperature, time, and the concentration of mercury bromide. The *N*-glucoside (XVII) was also isolated in a small amount when compound (XVI) was synthesised from the silver salt (XV).

The O → N rearrangement was studied using different Lewis acids[58]. When the pyridyl β-*O*-glucoside (XVI) was treated with tin(II) chloride, both anomerisation and rearrangement took place, while in the presence of $HgBr_2$ as the catalyst the anomerisation occurred virtually without rearrangement. The crystalline α-*O*-glucoside (XVIII) was obtained only when $HgBr_2$ was used as a catalyst, while in the presence of other Lewis acids the formation of the α-anomer was detected only by paper chromatography. The amount of the α-anomer formed when various catalysts are used decreases in the following sequence: $HgBr_2 > ZnBr_2 > CdCl_2 > SnCl_4 > SbCl_5 > TiCl_4$.

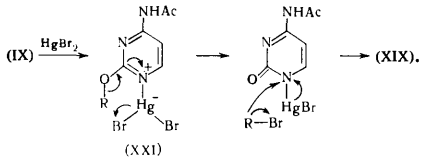
N-Acetylcytosinyl *O*-glucoside (XIX) also undergoes a rearrangement under the influence of tin(II) chloride to the β-*N*-isomer (IX) (mechanism C) but anomerisation was not observed under these conditions. The O → N glycosyl rearrangement catalysed by heavy metal salts ($SnCl_4$, $HgCl_2$, $HgBr_2$) was achieved by Schmidt and Farkas[46] [the di-*O*-glycosides of thymine (XIb) were converted into

thyminyl mono-*N*-glycosides (Xb)]. The thermal O → N glycosyl rearrangement of the readily hydrolysed *O*-glycoside 2-(tetra-acetyl-β-D-glucopyranosyl)hydroxypyrimidine was described recently[61]. The finding that in many cases the β-*O*-glycoside anomerises to the α-*O*-glycoside, while the α-*N*-isomer is not detected and that the rearrangement and the anomerisation take place at different rates and in different ways under different reaction conditions confirmed that two different mechanisms can operate in this case: (a) the formation of a complex of the catalyst and an oxygen atom of the sugar ring with subsequent ring opening and closure (anomerisation, mechanism A) and (b) the formation of a complex of the catalyst and the glycosidic oxygen, the formation of an ion pair, and the involvement of the adjacent 2-acyloxy-group (stereospecific rearrangement, mechanism B):



According to Wagner[59], the two products (XVII) and (XVIII) can be formed from the cyclic ion (XX), but in this case it is difficult to account for the formation of the α-*O*-glucoside and the absence of the α-*N*-glucoside.

The mechanism of the O → N glycosyl rearrangement, proposed previously by Ulbricht[36,38,56] and involving the formation of a complex of the catalyst with the ring nitrogen atom of the aglycone (XXI), was shown[61-65] to be inapplicable in all cases.

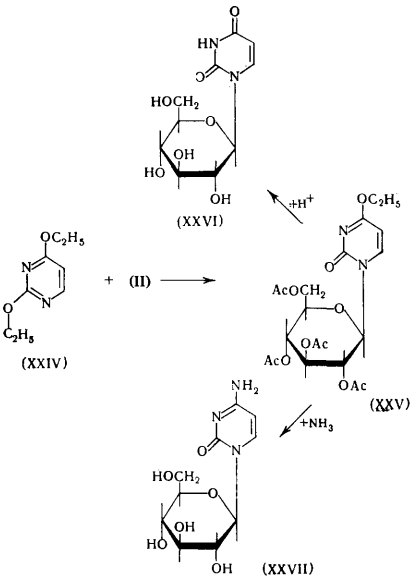


(R = 2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl)

III. THE HILBERT–JOHNSON METHOD

Previously it was believed that the glycosylation of the $N_{(1)}$-pyrimidine ring atom is impossible with pyrimidines containing the lactam—lactim tautomeric system $-\overset{\|}{C}(O)-\overset{|}{N}(H)- \rightleftharpoons -\overset{|}{C}(OH)=N-$. However, Hilbert and Johnson[66,67], who restricted the tautomeric shift by employing 2,4-dialkoxypyrimidines, extended this reaction to *O*-acylglycosyl halides[45] after the successful synthesis of 4-alkoxy-1-methyl-2(1*H*)-pyrimidinone (XXIII) by treating 2,4-dialkoxypyrimidine (XXII) with methyl iodide.

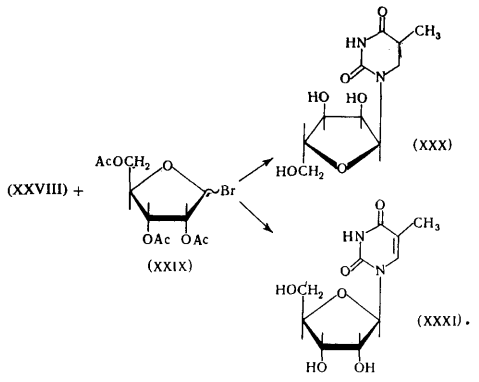
Thus, when 2,4-diethoxypyrimidine (XXIV) was treated with acetobromoglucose (II) (50°C, 48 h in the absence of a solvent), the $N_{(1)}$-glycosyl derivative (XXV) was obtained:



Treatment of compound (XXV) [45,68] with a solution of hydrogen chloride in ethanol or with a solution of ammonia in ethanol leads to the D-glucosides of uracil (XXVI) or (cytosine (XXVII). Many years later, Davoll et al.[69] reproduced these experiments[45,68] and established that the compounds obtained have the β-configuration.

Subsequently the reactions of 2,4-diethoxypyrimidine with L-arabinopyranosyl bromide, α-D-xylopyranosyl bromide, D-ribopyranosyl bromide, and α-D-galactopyranosyl bromide were carried out[70]. The first natural nucleoside obtained by the Hilbert–Johnson reaction was cytidine[71]. Its successful synthesis gave rise to further studies on the synthesis of pyrimidine nucleosides. For example, when 2,4-diethoxy-5-methylpyrimidine (XXVIII) was treated with 2,3,5-tri-*O*-acetyl-D-ribofuranosyl bromide (XXIX) (at 60°C in the absence of a solvent), "5-methyluridine" (A) (XXX) was isolated after hydrolysis[72]. In contrast to compound (A), the thymine nucleoside (C) obtained enzymatically from thymine and ribosyl phosphate was cleaved by the nucleosidase from *Escherichia Coli* and had a different melting point. 5-Methyluridine (C), synthesised later by the mercury method[29], was found to be identical with compound (B). By converting compound (C) into spongothymidine [1-(β-D-arabinofuranosyl)thymine],[74] the β-configuration of compounds (B) and (C) was demonstrated. Compound (A) was identified as the α-anomer[75] and it was observed that 1-(α-D-ribofuranosyl)thymine (XXX) and 1-(β-D-ribofuranosyl)thymine (XXXI) are obtained in yields of

8.5 and 8% respectively when the reaction is carried out in benzene:

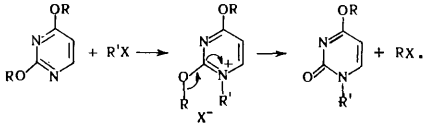


A mixture of 1-(α-D-ribopyranosyl)thymine and 1-(β-D-ribopyranosyl)thymine was obtained similarly from 2,3,4-tri-*O*-benzoyl-D-ribopyranosyl bromide [76].

Recently Sorm and coworkers [77] made a systematic study of the Hilbert–Johnson reaction. They investigated the role of the solvent, of various substituents in the 5-position of the pyrimidine ring, and of various protecting groups in the sugar component and studied the reaction yield and the ratio of the α- and β-anomers.

1. Reaction Mechanism

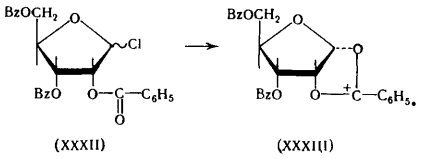
The reaction of 2,4-dialkoxypyrimidines with halogenoses (or with alkyl halides) was shown by Hilbert [78] to involve the formation of a quaternary salt as an intermediate. Later the mechanism of the Hilbert–Johnson reaction was investigated by Ulbricht [79]. His mechanism involves the formation of a quaternary nitrogen atom with subsequent attack by the halide ion:



It was shown recently [80] that a 2-alkoxy-group in the quaternary salt may be replaced by 2-oxo, 2-thio, and 2-amino-groups.

2. Stereochemistry of the Hilbert–Johnson Reaction

The effect of various factors on the ratio of the α- and β-anomers obtained by the Hilbert–Johnson reaction was investigated by Sorm and coworkers. The first papers [77,81] of this series were devoted to the synthesis of 2-deoxyuridine and thymidine, where the α-anomer predominates (for deoxy-sugars). It was established that the ratio of the α- and β-anomers in the Hilbert–Johnson method depends on the polarity of the solvent [81,82]. If, for example, the reaction of the halogenose (XXXII) with the base is carried out in benzene, a small amount of the corresponding α-anomer accompanies the main reaction product—the β-anomer. On the other hand, in a polar solvent the halogenose (XXXII), which is predominantly present in the β-configuration, gives rise to the ortho-ester cation (XXXIII), from which only the β-anomer may be formed.



The formation of the anomers is also influenced by the nature of the base and of the sugar component and by the protecting groups in the sugar residue [9]. Baker's "*trans*-rule" [52,53] is of limited applicability in the Hilbert–Johnson reaction, a mixture of α- and β-anomers being usually reformed.

3. Conditions of the Hilbert–Johnson Reaction

The absence or presence of the solvent plays an important role in the Hilbert–Johnson reaction. Best results are largely obtained in the presence of solvents although unfortunately systematic studies have not so far been made on this question. The reactions are carried out at temperatures ranging from 20° to 115°C. The reaction time was varied very markedly by investigators depending on the stability and reactivity of the halogenose employed. For example, the Hilbert–Johnson reaction of 2,4-dimethoxypyrimidine (in acetonitrile at room temperature) with 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-ribofuranosyl chloride requires 1–2 h, [83] while the reaction mixture with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl chloride must be kept for several days [81,82]. If the halogenose is relatively stable and less reactive, the reaction must be carried out at an elevated temperature, for example in a boiling solvent, while with a reactive and relatively unstable halogenose the condensation is carried out at room temperature.

The application of molecular sieves [82–86] as hydrogen chloride acceptors gave satisfactory results because the formation of side products was largely suppressed. The use of mercury bromide (in acetonitrile and benzene) was recently investigated [82,84,86]. Thus, when compound (XXII) reacted with 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-ribofuranosyl chloride, the rate of reaction was higher in the presence of one or two equivalents of mercury bromide, but the yield of the anomer mixture was appreciably reduced owing to the rapid decomposition of the deoxyhalogenose. The amount of the β-anomer in the mixture increases under these conditions. In the reactions with stable halogenoses, the use of mercury(II) bromide gives rise to the possibility of reducing the reaction time (without lowering the yield) [86].

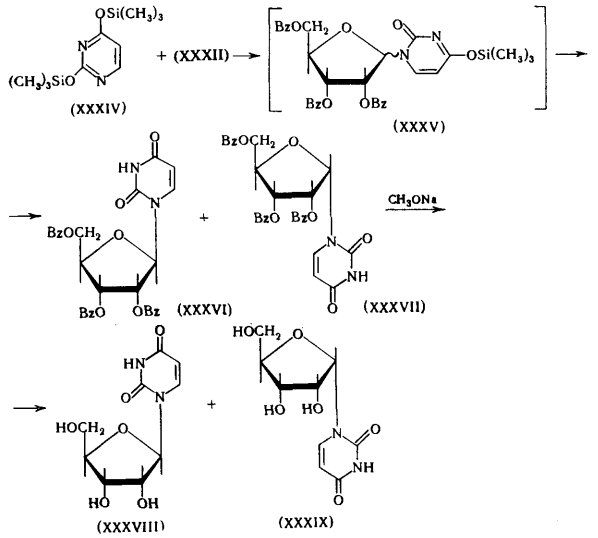
The side products usually formed in the Hilbert–Johnson reaction can be divided into four groups [9]: (1) substances obtained from the bases [for example uracil, 1-alkyluracils [45,70], 1,3-dialkyluracils [83], 4-alkoxy-2(1*H*)-pyrimidinones, and 4-alkoxy-1-alkyl-2(1*H*) pyrimidinones [70,84] may be formed from 2,4-dialkoxypyrimidines]; substances formed from the sugar component [84]; (3) side products obtained from the protected intermediate 4-alkoxy-1-glycosyl-2(1*H*)-pyrimidinones; (4) the *O*-glycosides mentioned above (they were first reported by Hilbert and Rist [87], who called them "*O*-nucleosides").

IV. THE TRIMETHYLSILYL METHOD

The trimethylsilyl method of synthesising nucleosides, the principle of which was discovered by Birkofer and coworkers [88-91] in studies on other nitrogen-containing compounds, was described by Nishimura and coworkers [92-97] and independently by Wittenburg [98-103]. The method is a modification of the Hilbert–Johnson method, but has a number of advantages. Silyl derivatives of pyrimidine bases can be obtained in high yields directly from pyrimidines such as uracil, thymine, and cytosine, the silyl derivatives being able to react with halogenoses under more severe conditions than their alkoxy-analogues. Compared with the Hilbert–Johnson method, the stage involving the hydrolysis of the alkoxy-group is virtually eliminated (the trimethylsilyl group is readily split off on treatment with aqueous alcohol).

Pyrimidine bases are sparingly soluble in organic solvents and have fairly high melting points. Their trimethylsilyl derivatives are liquids which can be distilled or crystals with a low melting point. Moreover, they dissolve readily in non-polar solvents, being completely decomposed by alcohol or water even in a neutral medium with liberation of the base.

The products of the silylation of dihydroxypyrimidines have the structure of bis-*O*-trimethylsilyloxypyrimidines (XXXIV).[92] The conversion of uracil into uridine (XXXVIII) and its anomer (XXXIX) may serve as an illustration of the trimethylsilyl method for the synthesis of nucleosides:



On treatment with chlorotrimethylsilane, uracil is readily converted into 2,4-bis(trimethylsilyloxy)pyrimidine (XXXIV) which on fusion (190°C) with 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl chloride yields the protected nucleoside (XXXV); on dissolution in ethanol the latter gave a benzoylated nucleoside in the form of a mixture of anomers (XXXVI) and (XXXVII). They were separated and deacylated with formation of uridine (XXXVIII) and 1-(α-D-ribofuranosyl)uracil (XXXIX).

Using the trimethylsilyl method for the synthesis of nucleosides, Wittenburg suggested the following versions of the condensation reaction [98,102]. Method A: prolonged heating of the components in dry solvents such as benzene, toluene, dimethylformamide (DMF), nitromethane, and others; method B: fusion of the components at 90–100°C *in vacuo*; method C: reaction carried out in an absolute inert solvent (benzene) in the presence of silver perchlorate at room temperature; method D: interaction of the starting materials at room or elevated temperature in a solvent in the presence of mercury(II) compounds, such as HgO, mercury(II) acetate, $HgBr_2$, and $HgCl_2$.

These methods were investigated in the reaction of 2,4-bis-*O*-trimethylsilylthymine with α-acetobromoglucose and β-acetochloroglucose. The yields were 27 and 41% by methods A and B and 56–86% by methods C and D. The use of polar solvents (DMF, acetonitrile) in method A accelerates the reaction but lowers the yield owing to the easier decomposition of the halogeno-sugars.

The technique of the fusion method B resembles that of the Hilbert–Johnson reaction. On fusion of bistrimethylsilylthymine with acetobromoglucose at 110°C, the reaction begins after several minutes and terminates after 1–3 h. The yield increases when the reaction is performed in benzene in the presence of one equivalent of silver perchlorate (method C). The reaction proceeds very rapidly even at room temperature and heat is evolved. Presumably silver perchlorate initially reacts with acetobromoglucose to form silver bromide and tetraacetylglucosyl perchlorate ($AgClO_4$ and silylpyrimidine do not react with one another) [91]. Since acetylglucosyl perchlorate is highly reactive [104], a further reaction with formation of a 4-*O*-silylnucleoside and trimethylsilyl perchlorate takes place.

The reaction in which mercury compounds are used as catalysts [HgO, mercury(II) acetate, $HgBr_2$, $HgCl_2$] (method D), particularly when an almost equimolar mixture HgO and $HgBr_2$ is employed, takes place more smoothly. The bromotrimethylsilane formed initially is converted into hexamethyldisiloxane in the presence of mercury(II) oxide and the acetylated products is isolated in a very satisfactory yield in consequence of a shift of the reaction equilibrium.

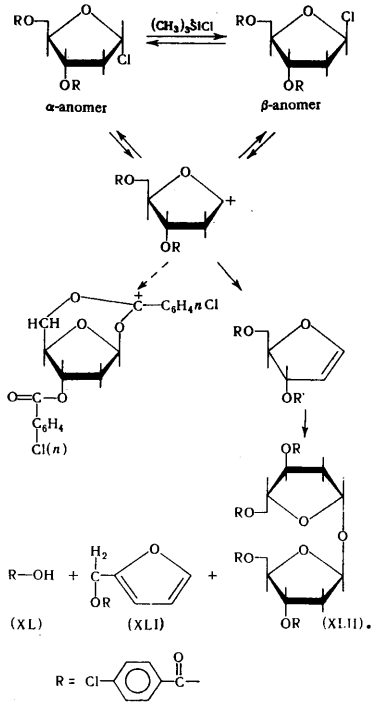
Wittenburg, who investigated the glycosylation of silyl derivatives of 6-substituted uracil derivatives [105] (6-methyluracil, 5,6-dimethyluracil, 5-bromo-6-methyluracil, 5-iodo-6-methyluracil, barbituric acid, and orotic acid and its esters) with acetobromoglucose or tribenzoylribofuranosyl chloride (method D was employed for glycosylation), concluded that the course of the reaction depends on the nature and position of the substituent in the pyrimidine ring. For example, in the glycosylation of the silyl derivative of 5,6-dimethyluracil under the above conditions, the $N_{(1)}$-glycoside was obtained almost exclusively, while in the reaction with 6-methyluracil the $N_{(3)}$-glycoside was formed preferentially together with appreciable amounts of the $N_{(1)}$-glycoside and the $N_{(1,3)}$-diglycoside. Other silyl derivatives listed above do not react with halogeno-sugars or with methyl iodide under the above conditions. Winkley and Robins [106] obtained similar results with silyl derivatives of 5,6-dimethyluracil and 6-methyluracil.

In this connection, it is noteworthy that the required $N_{(1)}$-glycosides of 6-methyluracil, barbituric acid [107], and orotic acid [108] were not obtained by the Hilbert–Johnson method either. However, Winkley and Robins [109] succeeded in synthesising 1-(β-D-ribofuranosyl)barbituric acid by the silyl method via condensation in acetonitrile at room temperature. Azacytidine [110], 2-deoxy-5-hydroxymethyluridine [111], and other derivatives of pyrimidine bases [112] were synthesised under these conditions.

Vorbruggen and Niedballa [113-115] suggested that the silyl derivative of pyrimidine bases be condensed with protected sugars in the presence of the Friedel–Krafts catalyst.

Stereochemical aspects. According to Wittenburg's data[102], a nucleoside with the $C_{(1)}-C_{(2)}$-*trans*-configuration was isolated as the main product in the interaction of 2,4-bis-(*O*-trimethylsilyl)thymine with α-acetobromoglucose. Traces of the α-anomer with the $C_{(1)}-C_{(2)}$-*cis*-configuration (i.e. traces of tetra-acetyl-α-D-glucopyranosylthymine), which proved to be identical with the α-glucopyranosylthymine obtained by Schmidt[46] by a modified Hilbert–Johnson method, were detected only in experiments by methods C and D. Treatment of bis-(trimethylsilyl)thymine with β-acetochloroglucose led to the same results. Hence Wittenburg concluded (without taking into account the amount of the anomers, which were detected by the chromatographic method alone) that the silyl method for the synthesis of pyrimidine nucleosides is rigorously stereospecific and fully obeys Baker's rule[52,53]. Nevertheless Nishimura and coworkers isolated α- and β-nucleosides[95,97] using adenine[96], uracil[95,97], and thymine[97] as aglycones. The Japanese workers concluded that the silyl method yields not only the β-anomers but also the α-anomers having the $C_{(1)}-C_{(2)}$-*cis*-configuration. Probably the formation of anomeric nucleosides depends to a very large extent on the reaction conditions (temperature, solvent, and catalyst).

A study of the factors influencing the stereospecificity of the silyl method for the synthesis of deoxynucleosides was made using as an example the reaction of 3,5-di-*p*-chlorobenzoyl-2-deoxy-α-D-ribofuranosyl chloride with the silyl derivatives of 5-mercaptouracil and thymine[116]. It was established that chlorotrimethylsilane has a major influence on the stereospecific course of the reaction. Under reaction conditions promoting the rapid removal of chlorotrimethylsilane from the reaction medium, the β-anomer is formed preferentially or exclusively. On the other hand, the addition of chlorotrimethylsilane to the reaction mixture promotes the formation of the α-anomer. It was found that chlorotrimethylsilane can cause the anomerisation of the halogenose under the reaction conditions;



To investigate the influence of chlorotrimethylsilane on the glycosyl chloride, the latter was allowed to stand in benzene in the presence and absence of chlorotrimethylsilane for several hours at room temperature. When the halogenose was allowed to stand for a long time in the absence of chlorotrimethylsilane in benzene solution (see scheme above), a small amount of compound (XLII) was isolated in addition to *p*-chlorobenzoic acid (XL) and furfuryl-*p*-chlorobenzoic acid. A carbonium ion can participate as an intermediate in the formation of all the degradation products of the glycosylhalogenose; the presence of chlorotrimethylsilane prevents the formation of the carbonium ion, stabilising the halogenose in the form of an equilibrium mixture of α- and β-anomers. In the condensation reaction, β-halogenose reacts much faster with bistrimethylsilylpyrimidine than the α-anomer and, as the latter is consumed, chlorotrimethylsilane is used to restore the equilibrium with inversion of the α-anomer to the β-anomer. Chlorotrimethylsilane does not anomerise the complete nucleoside.

Consequently the stereospecific formation of α- or β-deoxynucleosides can be explained solely on the basis of an S_N2 mechanism. Bearing in mind that the condensation reaction involves a nucleophilic attack by silylpyrimidine on glycosyl chloride with a single Walden inversion, the reaction of the pure α-halogenose should lead to the formation of the β-nucleoside; on the other hand, the reaction of the β-halogenose should tend to form the α-nucleoside.

Japanese workers found that, when bis(trimethylsilyl)-uracil and tribenzoylribofuranosyl chloride are fused together[95], bis(tribenzoylribosyl)uracil is formed together with the α- and β-anomers. The ultraviolet absorption spectrum of the debenzoylated product resembles that of 1,3-dimethyluracil[117]. However, the *O*-glycosides[102] formed when the mercury method is employed were not detected in the silyl method. Possibly, in the condensation of *O*-silyl derivatives with halogeno-sugars, there is a very fast migration of the sugar residue from the oxygen atom to the nitrogen atom with formation of an *N*-glycoside.

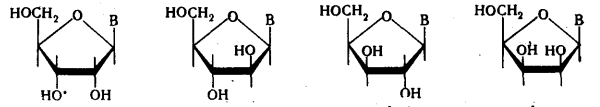
V. METHOD INVOLVING THE MODIFICATION OF THE SUGAR OR BASE IN THE COMPLETE NUCLEOSIDE

In nucleoside chemistry, there are many examples of reactions of nucleosides which involve changes both in the aglycone (halogenation, methylation, introduction of sulphur, deamination, etc.) and in the sugar component of the nucleoside, associated with the formation of anhydronucleosides (for example, a change in the configuration of the sugar residue or the introduction of a new functional group into the sugar moiety). Moreover, the changes in the aglycone are frequently results of the formation of anhydronucleosides.

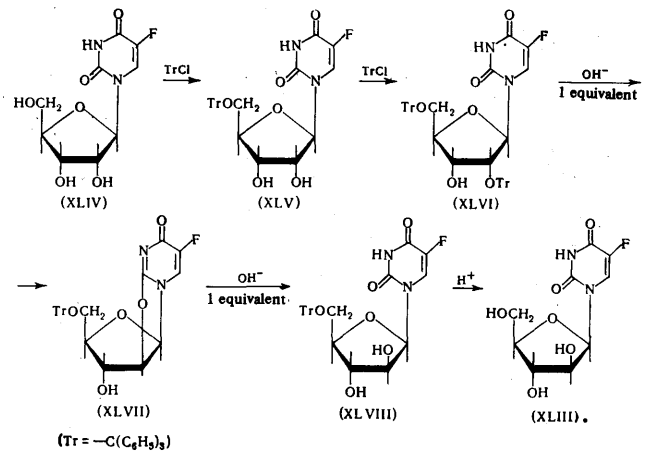
1. Transformations of Pyrimidine Nucleosides via Anhydronucleosides

The inversion of a hydroxy-group of the sugar was first described for thymidine; it occurred as a result of the formation of the 2,3′-anhydronucleoside, which is converted into 1-(β-D-deoxyxylofuranosyl)thymine on alkaline hydrolysis[118]. Subsequently similar results were obtained with ribonucleosides from which pyrimidine

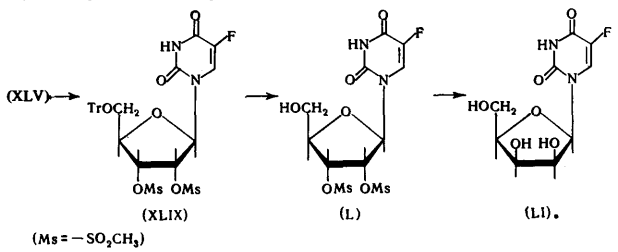
nucleosides with *lyxo*-, *xylo*-, and *arabino*-configurations are formed via the 2,2'- and 2,3'-anhydronucleosides.



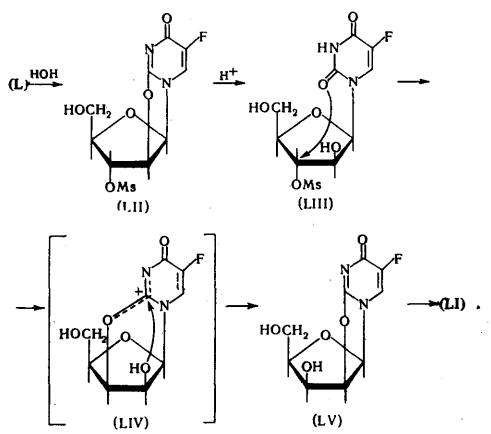
Thus 1-(β-D-arabinofuranosyl)urasil (spongouridine) [119] and 1-(β-D-arabinofuranosyl)thymine [120] were obtained in this way via the 2,2'-anhydronucleoside. A scheme for the synthesis of 1-(β-D-arabinofuranosyl)-5-fluorouracil (XLIII) [121] from 1-(β-D-ribofuranosyl)-5-fluorouracil (XLIV) via the trityl derivatives (XLV)–(XLVIII) is presented below:



When 5-fluoro-5'-trityluridine (XLV) was treated with methanesulphonyl chloride, 2',3'-dimethanesulphonyl-5'-tritylribofuranosyl-5-fluorouracil (XLIX) was obtained, its detritylation yielding the riboside (L); the removal of the methanesulphonyl groups by heating in water gave rise to 1-(β-D-lyxofuranosyl)-5-fluorouracil (LI):

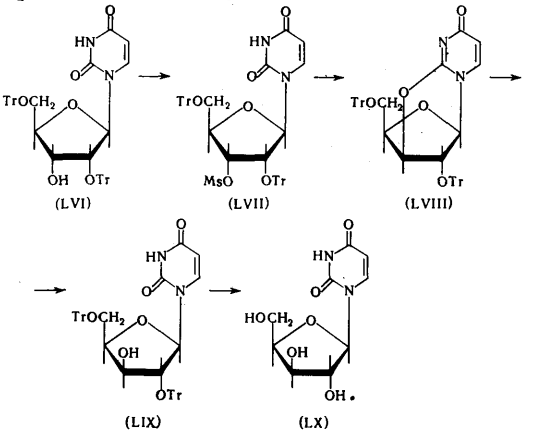


Compound (L) is converted into compound (LI) via a series of successive reactions [122]:

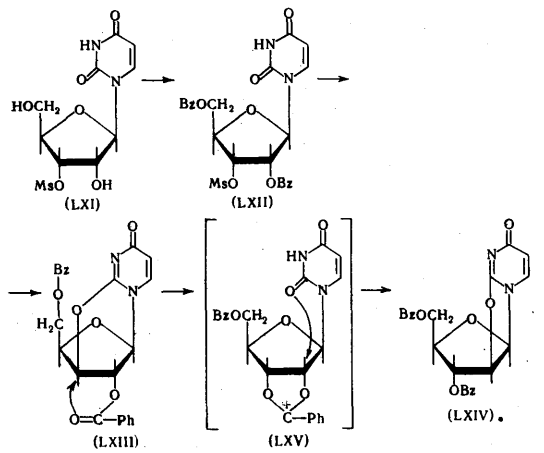


The first stage is the formation of the 2,2'-anhydronucleoside (LII) with liberation of methanesulphonic acid; next, in the presence of an acid catalyst, compound (LII) is cleaved to (LIII) and nucleophilic attack by the 2-carbonyl group on the $C_{(3)}$ carbon atom of the latter yields the 2,2'-anhydrolyxonucleoside (LIV). It is converted into the 2,2'-anhydrolyxonucleoside (LV) as a result of the attack by the OH group at $C'_{(2)}$ on the carbonium ion (LIV). Hydrolysis of compound (LV) leads to (LI).

3-*O*-Methanesulphonyl derivatives of uradine are frequently employed to obtain 2,3'-anhydronucleosides, which are intermediates in the synthesis of both xylofuranosyl and arabinofuranosyl nucleosides [123]. Tritylation of uridine under appropriate conditions leads to crystalline 2',5'-di-*O*-trityluridine (LVI) which on methanesulphonation is converted into 3'-*O*-methanesulphonyl-2',5'-di-*O*-trityluridine (LVII). On treatment with sodium benzoate in dimethylformamide, (LVII) is converted into 2,3'-anhydro-2',5'-di-*O*-tritylxylonucleoside (LVIII). Its treatment with alkali and subsequent detritylation yields a single product—1-(β-D-xylofuranosyl)uracil (LX).



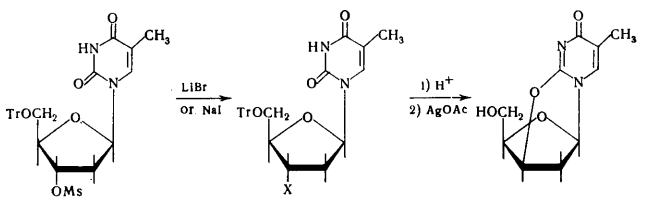
Detritylation of (LVII) yielded 3'-*O*-methanesulphonyluridine (LXI), the 3',5'-dibenzoyl derivative (LXII) of which gave the 2,3'-anhydroxylonucleoside (LXIII) on treatment with sodium benzoate [compound (LXIII) can be obtained also by the direct benzoylation of 2,3'-anhydroxylosyluracil]. When the anhydroxylonucleoside (LXIII) is heated up to its melting point, it isomerises rapidly to 2,2'-anhydro-3',5'-di-*O*-benzoylarabinonucleoside (LXIV), probably via a stage involving the formation of the orthoester ion (LXV) with participation of the adjacent acyl group.



The anhydronucleosides of pyrimidines proved to be convenient not only for the specific inversion of the hydroxy-groups of the sugar but also in the synthesis of 2-deoxynucleosides. Treatment of 5′-*O*-acetyl-2′-*O*-tosyluridine with sodium iodide leads to 5′-*O*-acetyl-2′-deoxy-2′- iodouridine from which 2-deoxyuridine is formed after hydrogenation and deacetylation [124]. The same iodo-derivative (with the ribose configuration) was obtained by treating with sodium iodide and acetic acid the 5′-*O*-acetyl-2,2′-anhydroarabinonucleoside, which can be formed from the iodo-derivative under the influence of a base [125]. Probably the anhydronucleoside is an intermediate in the substitution of toluene-*p*-sulphonyloxy-group by iodine, the final product being formed as a result of two substitutions at $C_{(2)}$.

Thymidine was synthesised by the same method from 5′-*O*-acetyl-1-(β-D-ribofuranosyl)thymine [124]. 2,3′-Anhydroxylonucleoside is the initial compound in the synthesis of 3′-deoxyuridine [126].

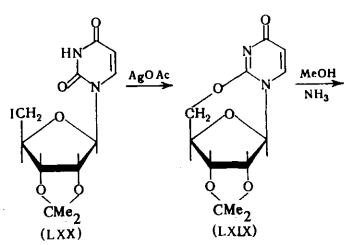
Anhydronucleosides can be used for the stereochemically controlled introduction of functional groups into secondary positions in the sugar residue. Michelson and Todd [118] synthesised 3′-deoxy-3′-halogenothymidine (LXVII) by treating 3′-methanesulphonyl-5′-tritylthymidine (LXVI) with sodium iodide or lithium bromide in acetone at 100°C. They suggested that (LXVI) has the *ribo*-configuration, since it can be inverted to give the 2,3′-anhydro-derivative (LXVIII):



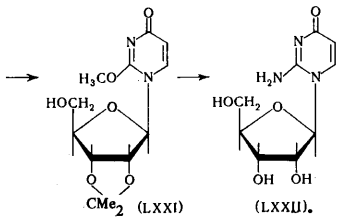
(LXVI) (X = Br, I) (LXVII) (LXVIII).

When 2,2′-anhydronucleosides are treated with anhydrous HBr, HCl, and HI, high yields of 2′-deoxy-2′-halogenonucleosides are formed [127]. It proved possible to obtain 3′-amino-3′-deoxythymidine and the 3′-deoxy-3′-phthalimidonucleoside from thymidine via the 2,3′-anhydro-derivative [128,129].

Anhydronucleosides are also used to replace the oxygen atom at the $C_{(2)}$ atom of the base by various substituents. Brown et al. showed that, when 2,5′-anhydro-2′,3′-isopropylidineuridine (LXIX) obtained from compound (LXX) is treated with a methanol solution of ammonia, the isocytosine derivative (LXXII) is formed via the 2-methoxy-nucleoside (LXXI). [126,130] 1-(β-D-Arabinosyl)isocytosine was synthesised from 2,2′-anhydroarabinosyluracil under the same conditions. Sulphur can be introduced into the heterocyclic ring via the 2,2′- and 2,5′-anhydronucleosides.

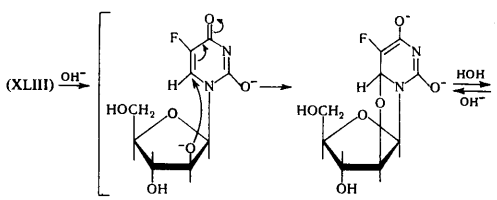


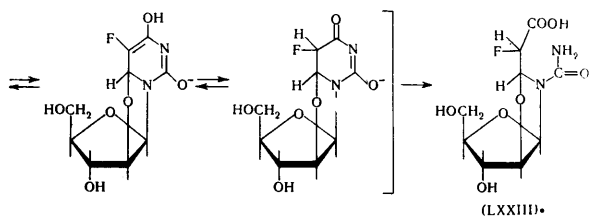
(LXX) (LXIX)



(LXXI) (LXXII).

Fox and coworkers made a detailed study of the behaviour of 5-halogeno-derivatives of spongouridine in an alkaline medium and showed that such nucleosides and their precursors (2,2′-anhydronucleosides) are unstable under these conditions [14,131-134]. For example, on treatment with alkali, 1-(β-D-arabinofuranosyl)-5-fluorouracil (XLIII) is converted into the 2′,6-anhydro-5-fluoro-5,6-dihydro derivative (LXXIII). It was suggested that the process proceeds via a 1,4-addition mechanism:

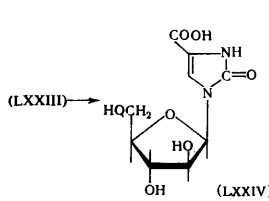




(LXXIII).

Compound (LXXIII) was one of the first products with a 2′,6′-anhydro-linkage obtained from nucleosides. The double bond is not reduced under the reaction conditions while the 3,4-bond is cleaved. The ease with which the 2′-OH anion having the *arabino*-configuration participates in the reaction is probably a property of pyrimidine nucleosides having the aglycone and 2′-OH in the *cis*-positions.

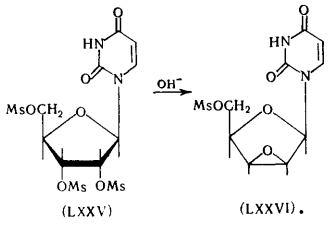
The study of the properties of the 2′,6-anhydro-5-fluoro-5,6-dihydro-derivative (LXXIII) led to the discovery of a new rearrangement of the aglycones of 5-halogeno-derivatives of arabinosyl nucleosides. The reaction of (LXXIII) with 1 *N* NaOH for 20 min at 60°C gives a crystalline halogen-free product (LXXIV):



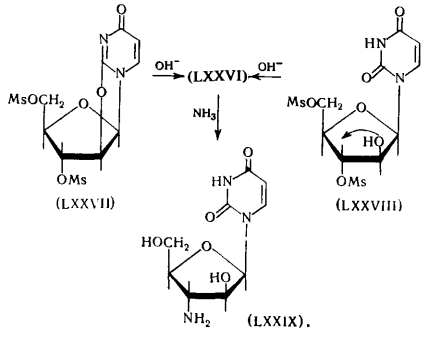
(LXXIV).

A possible mechanism of the conversion of (LXXIII) into (LXXIV) consists in the nucleophilic attack by the amide nitrogen on the $C_{(5)}$ atom with substitution of the fluorine and subsequent cyclisation, dehydrogenation, and cleavage of the 2′,6-anhydro-linkage [14,132]. Anhydronucleosides can be used to synthesise epoxy-derivatives

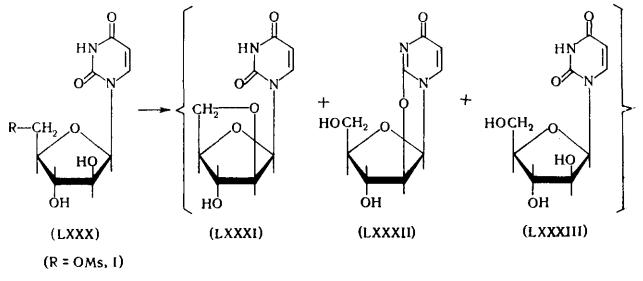
of nucleosides. Treatment of tri-*O*-methanesulphonyluridine (LXXV) with three equivalents of alkali gives a high yield of the 2′,3′-epoxide (LXXVI):[135,136]



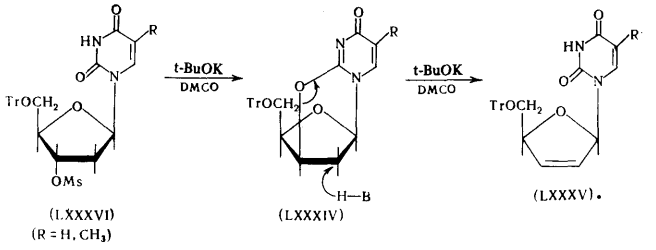
This reaction can probably proceed via the anhydronucleoside (LXXVII) and the arabinonucleoside (LXXVIII), since each is converted into an epoxide on treatment with alkali. On treatment with an alcoholic solution of ammonia at an elevated temperature, the epoxide is converted into 1-(3′-amino-3′-deoxy-β-D-arabinofuranosyl)uracil (LXXIX):[135]



In the course of a study of the hydrolytic cleavage of the 5′-iodo- or 5′-methanesulphonyloxy-derivatives of arabinosyluracil, evidence was obtained for intramolecular reactions involving anhydronucleosides[137]. Treatment of compound (LXXX) with boiling water results in the formation of three products: 2′,5′-epoxynucleoside (LXXXI), 2,2′-anhydronucleoside (LXXXII), and 1-(β-D-arabinofuranosyl)uracil (LXXXIII). The last compound can be obtained by the hydrolysis of (LXXXII).

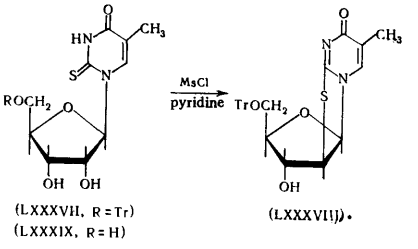


Recently Horwitz and coworkers showed[138,139] that certain anhydronucleosides can be used to synthesise derivatives unsaturated in the sugar moiety by a base-catalysed elimination reaction. Thus, on treatment with potassium t-butoxide in dimethyl sulphoxide (DMSO), the anhydronucleoside (LXXXIV) gives rise to a high yield of the Δ2′,3′-nucleoside (LXXXV), which can also be obtained from the nucleoside (LXXXVI) under the same conditions:

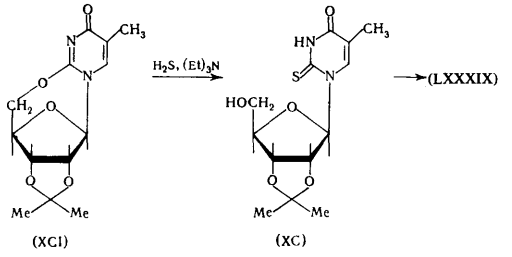


Detritylation of compound (LXXXV) yields "thymidinene" and "uridinene" respectively.

The first synthesis of an anhydronucleoside containing a sulphur atom instead of oxygen in the anhydride bridge was achieved by Shaw and Warrener, who observed that the $S_{(2)}$, 2′-anhydronucleoside (LXXXVIII) is formed in high yields on methanesulphonation of 5-methyl-2-thio-5′-*O*-trityluridine (LXXXVII).[140,141]

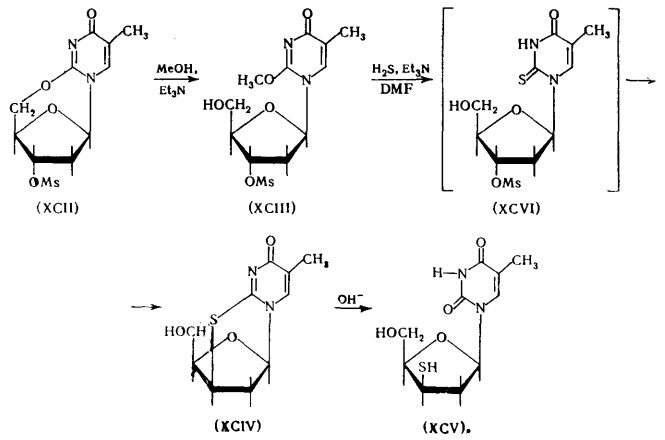


The initial compound (LXXXVII) was obtained by the tritylation of the thionucleoside (LXXXIX), which was synthesised from isopropylidene-2-thiouridine (XC), one of the products of the interaction of 2,5′-anhydro-2′,3′-isopropylideneuridine (XCI) with hydrogen sulphide in the presence of triethylamine:



When the 2,5′-anhydronucleoside (XCII) is heated with methanol containing triethylamine, a high yield of the 2-methoxynucleoside (XCIII) is obtained; its treatment with hydrogen sulphide and triethylamine in DMF in 65°C for several hours leads to the $S_{(2)}$,3′-anhydronucleoside

(XCIV). The cleavage of the sulphide bridge with 0.1 *N* solution of alkali gives the 3′-mercaptonucleoside (XCV):



The 2-thionucleoside (XCVI), which was synthesised from compound (XCII) by treatment with hydrogen sulphide (in DMF) and triethylamine at room temperature, is an intermediate in the conversion of (XCIII) into (XCIV). Compound (XCVI) was converted into compound (XCIV) by refluxing in ethanol containing triethylamine.

The introduction of sulphur into the $C_{(4)}$-position in the pyrimidine ring is used as an intermediate reaction in the general method for the conversion of various uracil nucleosides into their cytosine analogues [142]. As a rule, treatment of uracil and its derivatives with phosphorus pentasulphide results in the introduction of the thio-group in the 4-position.

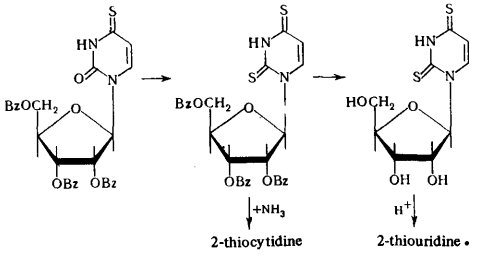
In model experiments with 1-methyluracil, the introduction of sulphur followed by amination yielded 1-methylcytosine; hence it was concluded that this reaction can be used also to synthesise nucleosides. In the latter case the hydroxy-groups of the sugar residue must be protected (with the benzoyl group) and pyridine must be employed as the reaction medium.

As a result of the introduction of the thio-group into ribo- and deoxyribopyrimidine nucleosides, reactive intermediates are obtained from which one can synthesise not only the principal natural nucleosides but also various 4-substituted analogues. Thus the 4-thio-compound was obtained from 3′,5′-di-*O*-benzoylthymidine and was converted by treatment with an alcoholic ammonia solution into 2-deoxy-5-methylcytidine. Uridine and 1-(β-D-ribofuranosyl)thymine were converted in this way into cytidine and 5-methylcytidine; likewise glycosyl-5-fluorocytosines were obtained from 5-fluorouridine and 2-deoxy-5-fluorouridine [143]. 5-Azacytidine is obtained in a similar way following the introduction of the thio-group into tri-*O*-benzoyl-5-azauridine with subsequent amination and debenzylation [144,145].

When acylated 4-thionucleosides (including 2-deoxy-derivatives) are treated with appropriate reagents, 4-alkylamino-, 4-hydrazino-, 4-hydroxylamino-, and other derivatives are formed [143].

When the thio-group in 4-thiothymidine and 4-thiouridine is removed with activated Raney nickel, the heterocyclic ring is fully hydrogenated with formation of 2-oxohexahydropyrimidine nucleosides. Such ready and extensive reduction is characteristic of 4-thiouracils and 2-hydroxypyrimidines and does not occur with 2-thiouracils and 4-hydroxypyrimidines [146].

Brown and Herper [147] succeeded in introducing sulphur directly at the $C_{(2)}$-position in 1-methyluracil by treatment with P_2S_5 in tetralin [147]. In 1968 Japanese workers achieved this reaction with the corresponding nucleosides [148]:



2. Halogenation of Nucleosides

In 1907 Wheeler and Johnson observed for the first time the decolorisation of bromine water by uracil and cytosine. Since then, this reaction has been used as a qualitative test for these substances. The colorimetric method for the determination of uracil and cytosine is also based on it [149]. The reaction likewise plays an important role in the synthesis of nucleoside derivatives, in particular 5-bromouridine [150].

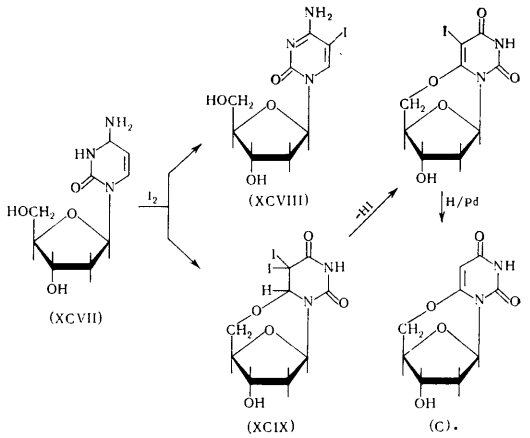
The halogenation of pyrimidine nucleosides takes place readily and leads to a modification of the heterocyclic ring without its cleavage. Usually nucleosides and bases are halogenated with the free halogen in an anhydrous solvent (the iodination reaction is an exception) in which substitution at the fifth carbon atom, where there is an excess of electron density, takes place [151-154].

The bromination of nucleosides usually occurs under very mild conditions and can be achieved in several ways: (a) in anhydrous solvents, for example in DMF, pyridine, formamide, and alcohol [155,156]; 5-bromo-derivatives of cytidine and deoxycytidine were obtained under the same conditions [155-157]; (b) with bromine water and subsequent lyophilisation [158] and (c) with simultaneous irradiation by ultraviolet light [159,160]. The mechanism of the halogenation reaction has been investigated in detail for the bromination of pyrimidine nucleosides [161-163].

As a rule uracil derivatives are chlorinated with a chlorine solution in dry carbon tetrachloride, which is added to a solution of the initial compound in glacial acetic acid. The reaction proceeds readily and terminates after several hours at room temperature or after several minutes on heating. It proved possible to obtain in this way 5-chlorouridine [158,164] and 5-chlorodeoxyuridine [165]. 5-Chlorocytidine cannot be obtained under similar conditions [159], because cytidine exists in a protonated form in glacial acetic acid and electrophilic attack is difficult. However, when the reaction mixture containing cytidine is irradiated by ultraviolet light, the reaction takes place smoothly, probably owing to a change in reaction mechanism, with radical substitution instead of electrophilic substitution.

The iodination of pyrimidine nucleosides takes place under much more severe conditions. Iodination methods have been developed and introduced into the synthetic chemistry of nucleosides by Prusoff [166,167]. The commonest iodination procedure involves heating the nucleosides with a chloroform solution of iodine in the presence of nitric acid. Modifications of this method consist in using different solvents, different nitric acid concentrations, or different heating times [166-170]. 5-Iodo-derivatives of uridine, deoxyuridine, etc. have been obtained in this way.

Another possible iodination procedure involves treatment with iodine in the presence of alkalis [166]. However, these methods cannot be used to synthesise 5-iodo-derivatives of cytidine and deoxycytidine, since under these iodination conditions the *N*-glycosidic bond is broken [171]. The replacement of nitric acid by another oxidising agent (for example iodic-acid) which does not affect the glycocidic linkage permits the successful iodination of cytidine and deoxycytidine (XCVII). [172] Together with deoxy-5-iodo-cytidine (XCVIII), a side product was isolated, which proved to be the anhydrodi-iodonucleoside (XCIX); the latter can be converted into the deiodinated product (C): [13]



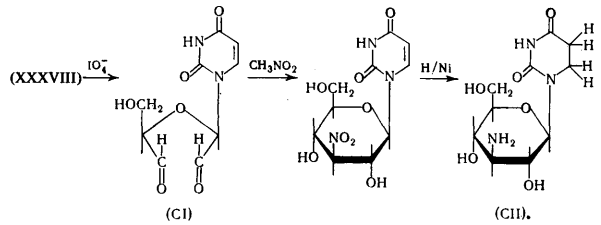
Bromine chloride and iodine chloride have been used as mild iodinating and brominating agents. Joshida et al. [173] believe that electrophilic substitution takes place in this case and suggest that in iodination and bromination by this method in DMF the formation of 5-halogenouridines is accompanied by the formation of 5-halogeno-5,6-dihydro-6-hydroxyuridine, as in bromination in aqueous solvents.

N-Halogenoamides and *N*-halogenoimides are effective halogenating agents, which made it possible to replace the hydrogen atom at the $C_{(5)}$-position of the pyrimidine ring under extremely mild conditions. Thus the use of *N*-chloro- and *N*-bromo-succinimides permits the synthesis of 5-chloro- and 5-bromo-derivatives in almost quantitative yields [174-180]. For iodination with *N*-iodo-succinimide in DMSO, it is necessary to add catalytic amounts of di-n-butyl disulphide [178,181], which is probably required to form an intermediate halogenating agent—n-butylsulphenyl iodide.

Fluorine-containing nucleosides are usually obtained from the corresponding fluoro-derivatives of pyrimidine using one of the direct methods of synthesis discussed above.

3. Oxidation of Nucleosides

Fox and coworkers [182] obtained nucleosides derived from 3'-amino-3'-deoxyaldoses by the periodate oxidation of uridine to the dialdehyde (CI) without the cleavage of the glycosidic linkage; the addition of nitromethane leads to cyclisation. 1-(3'-Amino-3'-deoxy-β-D-glucopyranosyl)-5,6-dihydrouracil (CII) was obtained after the reduction of the nitro-group:



Among the methods of synthesis of pyrimidine nucleosides discussed above, the silyl method is the most advantageous. This is clearly seen from the synthesis of 1-(β-D-xylofuranosyl)uracil and 5-bromouracil tribenzoates [183-187]. The yield of the first compound was 77% by the silyl method and 28% by the mercury method; in the synthesis involving the modification of the ribose residue of uridine, this compound was obtained in a yield of only 8%. [188]

As a preparative method, the modification procedure suffers from many disadvantages among which the large number of stages in the processes and the low yield of products are of primary importance. Nevertheless, this method permitted an appreciable expansion of the chemistry of nucleosides and led to the possibility of a wide variety of chemical transformations of the compounds.

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Sechenov Moscow Medical Institute

Institute of Biochemistry, USSR Academy of Sciences, Moscow

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Organosilicon Epoxy-compounds

L.V.Nozdrina, Ya.I.Mindlin, and K.A.Andrianov

The review deals with methods for the synthesis of monomeric organosilicon epoxy-compounds and some of their reactions. The possibility of employing these compounds for the synthesis of organosilicon polyepoxides is demonstrated and some of their properties are described.
The bibliography includes 46 references.

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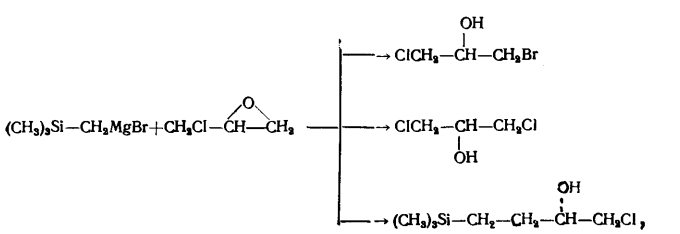
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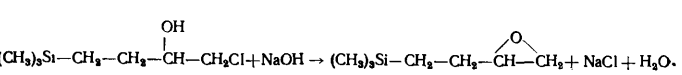
1. INTRODUCTION

Organosilicon polymers have found many applications in industry in view of their thermal stability and good dielectric properties. However, owing to their low mechanical strength and poor adhesion to glass and metals, the scope of their applications is significantly restricted. Materials formed on the basis of epoxy-resins are known to have a very high strength and satisfactory adhesion characteristics. Therefore at the present time much attention is being devoted to the synthesis of monomeric organosilicon compounds containing heterofunctional groups, particularly epoxy-groups, in the side chain at the silicon atom. Among the methods described for the synthesis of organosilicon epoxy-compounds, several trends may be distinguished.

2. DEHYDROHALOGENATION OF ORGANOSILICON CHLOROHYDRINS

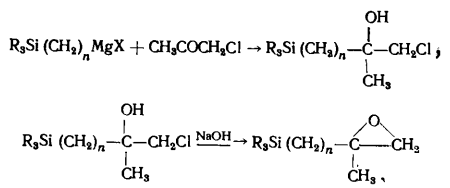
A widely employed method of synthesising epoxyalkanes is based on the dehydrohalogenation of halogenohydrins in the presence of alkaline agents. The first epoxysilylalkane was obtained by the interaction of the corresponding Grignard reagent with epichlorohydrin and subsequent dehydrohalogenation. The reaction resulted in a large amount of side products together with the desired substance:





The yields of the organosilicon chlorohydrins and of the corresponding epoxide did not exceed 25–30%.

The possibility of obtaining the halogenohydrin by the reaction of the Grignard reagent derived from the halogenoalkylsilane with monochloroacetone has been demonstrated[2]. The unambiguous course of this reaction makes it possible to obtain epoxides in high yields according to the scheme:



Ethynylepoxides have been obtained in this way[3,4].

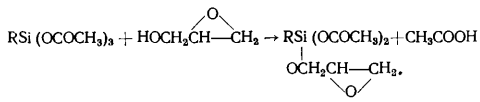
The attempt to obtain an epoxide from $R_2Si(OH)-CHCl-CH_3$ was unsuccessful[2]. Sodium hydroxide hydrolysed the Si–C bonds, while in the presence of calcium hydroxide the initial compound underwent no changes.

A method based on the addition of silanes to unsaturated halogenohydrins has also been used to synthesise organosilicon halogenohydrins. When trialkylsilanes react with $\delta\epsilon$-unsaturated halogenohydrins in the presence of H_2PtCl_6, products resulting from both addition to the multiple bond and dehydrocondensation are formed. The reaction of silanes with $\gamma\sigma$-unsaturated halogenohydrins yields only dehydrocondensation products[5,6].

3. REACTIONS OF FUNCTIONAL GROUPS AT THE SILICON ATOM WITH EPOXY-COMPOUNDS

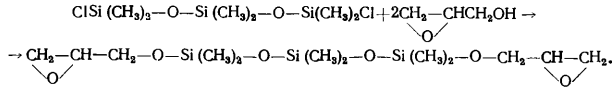
Tetra-alkoxysilanes (for example, tetraethoxysilane) or poly(silyl ethers) containing lower alkoxy-groups (methoxy-, ethoxy-) undergo complete or partial transetherification with glycidol *in vacuo* at a low temperature in the presence of transetherification catalysts (alkoxides)[7]. The compounds obtained readily harden on heating with maleic anhydride, forming polymers with satisfactory physicomechanical properties[8,9].

Acetoxyalkylsilanes also react with glycidol[10] forming glycidyl derivatives of silanes as follows:



With decrease of the number of acetyl groups in alkylacetoxysilanes, their replacement by glycidyl residues becomes more difficult. Thus the acetoxy-groups in triacetoxymethylsilane and triacetoxyvinylsilane are fully replaced by glycidyl groups, while in diacetoxydimethyl- and diacetoxymethyl-silanes they are replaced only to the extent of 70–75%; in triacetoxytrimethylsilane no substitution takes place at all.

Yamamoto[11] and Martin[12] isolated glycidylsilanes after allowing chlorosiloxanes to react with glycidol in the presence of tertiary amines as catalysts:



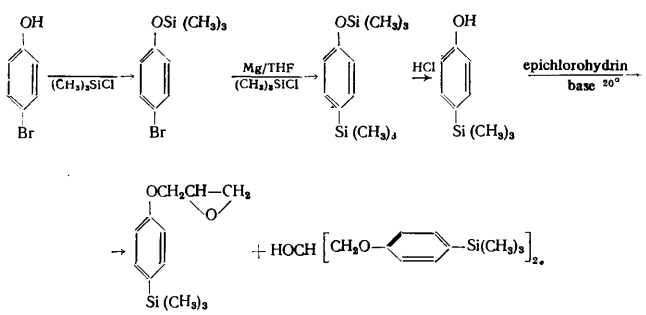
Rogers and Lewis[13] extended the scope of the synthesis of such silicon compounds. They suggested that glycidylsilanes be obtained by the reaction of glycidol or epichlorohydrin with organosilicon compounds containing not only halogeno-, alkoxy-, and acyloxy-groups at the silicon atom but also amino-, aryloxy-, and hydroxy-groups. The reaction is catalysed by alkali and is carried out at high temperatures. The resulting organosilicon epoxy-derivatives can be used as casting resins or for the preparation of laminated plastics.

Glycidylsilanes are hydrolytically and thermally unstable.

4. INTERACTION OF EPICHLOROHYDRIN WITH FUNCTIONAL GROUPS IN THE SIDE CHAIN AT THE SILICON ATOM

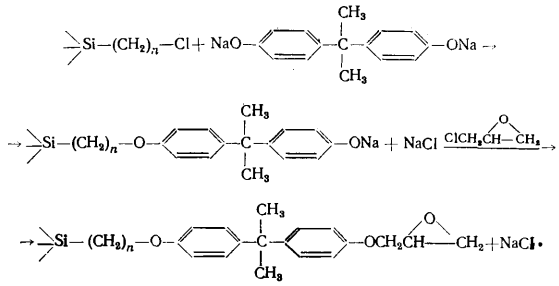
Aryl glycidyl ethers, obtained by the interaction of epichlorohydrin, aromatic hydroxy-compounds, and alkali, have become the main starting materials for the preparation of epoxy-resins. It was interesting to obtain the organosilicon analogues of such resins.

A report on the synthesis of glycidyl 4-trimethylsilylphenyl ether according to the following scheme has been published[14]:



Glycidyl 4-triphenylsilylphenyl ether has been synthesised in the same way[15].

Daniel[16] has proposed a convenient and simple method for the synthesis of interesting organosilicon derivatives of glycidol:



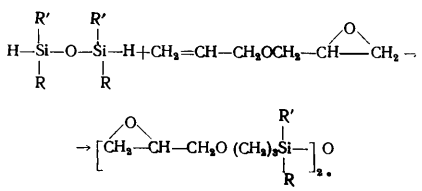
The initial organosilicon halides can be linear, cyclic or branched.

The polymers obtained from these monomers, which can be hardened by amines, are highly resistant to the action of chemical agents and have excellent adhesion properties and thermal stability. They are employed in engineering as insulating materials. Unfortunately the authors of this study do not quote quantitative estimates of the properties of the polymers.

5. ADDITION OF SILANES TO UNSATURATED EPOXY-COMPOUNDS

Silanes add to the double bonds of epoxyolefins in the same way as to other unsaturated compounds, in the presence of peroxide or platinum catalysts. The addition takes place under relatively mild conditions and the epoxy-group remains unchanged[17]. This reaction is applicable to silanes, alkoxysilanes, acyloxysilanes, and siloxanes, but not to chlorosilanes.

The attempt to isolate[18] $\alpha\omega$-bisepoxides after the reaction of allyl glycidyl ether with HRR'SiOSiR'RH in the presence of 0.1 *N* H_2PtCl_6 solution yielded polymeric products, probably as a result of the rupture of the epoxy-ring. It proved possible to obtain a bisepoxide of this kind by the following reaction using Pt/C containing 20% Pt as a catalyst:



By employing various epoxyolefins, it is possible to obtain a wide variety of organosilicon epoxides. In particular, Plueddemann and Fanger[17] obtained such compounds by the interaction of silanes with the monoepoxy-derivative of butadiene, allyl glycidyl ether, the monoepoxy-derivative of limonene, the monoepoxy-derivative of vinylcyclohexene, and 2-allylphenyl glycidyl ether. Other workers synthesised aminoepoxy-siloxanes[18–20], chlorine-containing organosilicon epoxides[21], and unsaturated organosilicon epoxy-derivatives[22]. Polymeric products derived from the latter can be obtained not only as a result of the opening of the epoxy-ring but also via the multiple bond.

Plueddemann[23] isolated individual cyclic, branched, and linear glycidylpropylsiloxanes containing less than six units. When these siloxanes hardened, it was found that cyclic polyepoxysilanes exhibit the highest hardness,

thermal stability, and impact strength. The Martens thermal stability of the polymers of lower epoxysilanes is lower than that of the usual epoxy-resins, but that of the higher polymeric epoxy-silanes is higher.

Epoxy-siloxanes synthesised by the addition of silanes have been recommended as active solvents for casting and adhesive epoxy-resins (in particular epoxynovolac resins[24]), as components of phenolic[25], alkyd, and polyester resins[26] to impart to them a higher thermal stability, as modifying agents for silicone resins to improve their adhesion and mechanical properties, and for other purposes. In 1958, epoxy-compounds of this kind were produced in France on an industrial scale[26].

6. OXIDATION OF UNSATURATED SILICON COMPOUNDS

Organosilicon epoxy-compounds with the smallest organic groups can be obtained by oxidising a multiple bond. The Prilezhaev epoxidation of silylolefins by peracids has been described. Organic peracids are electrophilic agents, the rate of reaction with such acids increasing appreciably as the nucleophilic properties of the olefin are enhanced following the substitution of the hydrogen atoms at the double bond by electron donating groups[27]. The silicon atom linked to the unsaturated aliphatic group should facilitate its oxidation by peracids.

Wende and Gesierich[28] showed that allyltriphenylsilane interacts with perbenzoic acid at a higher rate than the analogous carbon compound 1,1,1-triphenylbut-3-ene. The authors explained the increase of the rate of reaction by the negative charge on the double bond induced by the silicon atom. Under the same conditions, the vinylsilicon derivative reacts with a peracid (peracetic[17] and perbenzoic[28]) much more slowly than the allyl derivative.

In organosilicon compounds where the double bond is separated from the silicon atom by more than two carbon atoms, the silicon atom has no effect on the oxidation of the unsaturated group[17]. Organosilicon compounds containing two unsaturated groups[28] are oxidised faster than those containing one unsaturated group.

A study of the epoxidation of dimethyldivinylsilane with perbenzoic acid established[29] that the first vinyl group is oxidised much faster; the amount of monoepoxide formed is 5–6 times greater than that of the diepoxide.

In the oxidation of tetravinyldisiloxane, the first two vinyl groups are readily oxidised, while the third and particularly the fourth group are oxidised much more slowly.

When epoxy-rings accumulate in the molecule, the stability of the compound diminishes.

The general characteristics of the epoxidation reaction hold for unsaturated siloxane derivatives. The introduction into the silane molecule of the electrophilic phenyl group decreases the reactivity of the vinyl group at the silicon atom; the bulky trimethylsilyl group has a similar effect. On the other hand, when the small electron-donating methyl group is present, the rate of epoxidation increases[30].

The rate of oxidation of silanes containing one unsaturated group by perbenzoic acid decreases in the following sequence: trimethylsilane > tripropylsilane > triethylsilane > tribenzylsilane > triphenylalkylenesilane[28].

Numerous studies have established[31] that the rate of reaction between peracids and olefins follows a second-order equation (the reaction is of first-order with respect to each component). Kinetic data for the oxidation of the vinyl group in silylolefins by perbenzoic acid[30] have shown that the reaction involving organosilicon compounds is also of second order and can be represented by the following kinetic equation:

$$-\frac{dx}{d\tau} = k\,(C_3H_5CO_3H)\ \text{(silyl olefin)}.$$

The rate constant depends on the number and nature of the substituents in the reacting molecule and on the strength of the acid oxidising the olefin[32].

The epoxidation of unsaturated silicon compounds by perbenzoic[33–36], perphthalic[37], 40% peracetic[17], and peroxytrifluoroacetic[38] acids has shown that peroxytrifluoroacetic acid is the best epoxidising agent. The oxidation with perbenzoic acid is as a rule carried out at 0–20°C over a period of several days.

The epoxidation of vinylsiloxanes with 40% peracetic acid in acetic acid is very slow and gives a very low yield of epoxy-derivatives (less than 20%). Temperature and time play an important role. On raising the temperature and reaction time, there is an increased contribution due to decomposition side reactions and the yield of the epoxy-product falls appreciably[38]. Therefore one must employ the most reactive peracid and the optimal reaction conditions must be determined.

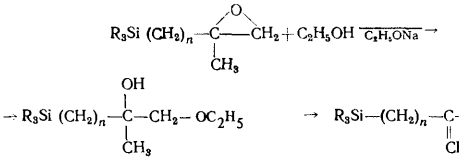
The reaction of unsaturated silicon compounds with perbenzoic acid takes place in chloroform and carbon tetrachloride much faster than in other solvents, but by employing a less active solvent (ether, tetrahydrofuran) it is possible to eliminate the side reactions.

Epoxy-organosiloxanes obtained by the oxidation of the vinyl group give rise to absorption bands in the infrared close to 758, 815, and 1138 cm^{-1}, which are characteristic of the epoxy-group[39]. Compounds of this class can be used as plasticisers, coatings, adhesives, and casting resins[39]. They are also suitable as agents imparting to coatings based on siloxanes an enhanced stability to wear[40].

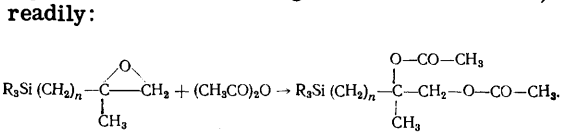
7. REACTIONS OF ORGANOSILICON EPOXY-COMPOUNDS

The epoxy-group in organosilicon compounds enters into its characteristic reactions with alcohols, phenols, acids, amines, and other compounds in the presence of appropriate catalysts[18,26,41].

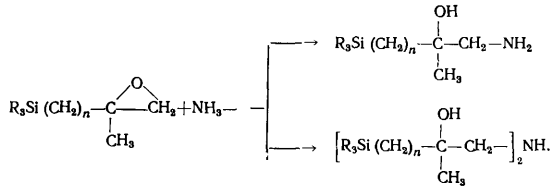
On treatment with alcohols in the presence of sodium alkoxides, organosilicon epoxy-compounds form ether-alcohols which are dehydrated on heating in the presence of $KHSO_4$ with formation of unsaturated organosilicon ethers[42]:



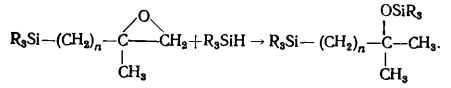
The reaction of epoxysilanes with acetic anhydride, resulting in the formation of organosilicon diacetates, takes place readily:



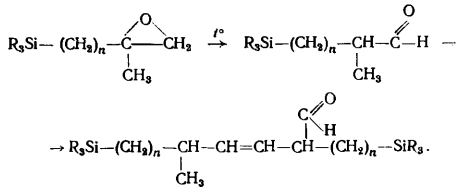
On prolonged refluxing of organosilicon epoxy-compounds with ammonia, organosilicon mono- and di-amino-alcohols are produced:



Organosilicon epoxy-compounds readily combine with silanes, forming an ether and not an alcohol[2]:

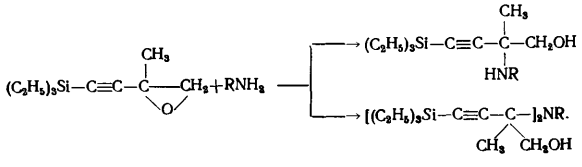


On prolonged heating up to the boiling point (at atmospheric pressure), organosilicon epoxy-compounds isomerise to aldehydes, which then undergo partial crotonic condensation[42]:

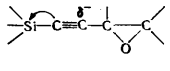


In order to assess the electronic influence of the silicon atom on the properties of the adjacent epoxy-group, a study was made of the reduction of a number of epoxyethylsilanes with lithium aluminium hydride[43]. In monosubstituted epoxides, the sterically more accessible carbon atom is usually subjected to hydride attack with formation of a secondary alcohol. When epoxyethylsilanes are reduced, a primary alcohol $R_3SiCH_2CH_2OH$ is formed unambiguously in a high yield. It would appear that steric factors should favour attack on the primary carbon atom in epoxyethylsilanes, but it has been established that in the reduction with lithium aluminium deuteride a primary alcohol is formed as a result of direct attack by the hydride ion on the carbon atom linked to silicon; this anomalous behaviour of epoxyethylsilanes can be explained by the electronic influence of the silicon atom on the epoxy-group.

The epoxy-ring of organosilicon ethynylepoxides[3], where the silicon atom is linked directly to a triple bond, is opened under the influence of aliphatic amines at the carbon atom linked directly to the triple bond (contrary to the Krasusskii rule):

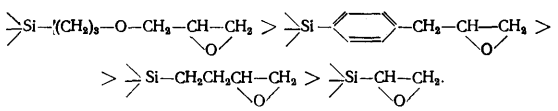


This phenomenon can be explained by a specific intramolecular interaction of the triple bond π electrons with the free *d*-orbital of the silicon atom, which leads to an enhanced polarisability of the C–O bond on the side of the more substituted carbon atom:

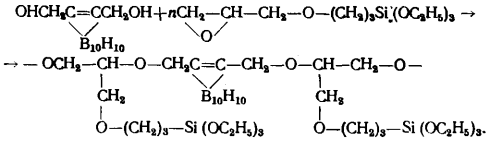


The proximity of the silicon atom lowers the reactivity of the epoxy-group in relation to the aromatic amine[44].

Organosilicon epoxy-compounds can be arranged in the following sequence in terms of their reactivity in the presence of the aromatic amine $H_2N-C_6H_4-OSi\equiv$ at 100°C:



Epoxy-organosilanes form optically active polymers[45] in the presence of a catalytic system comprising an organometallic compound and a complex-forming agent. A study of the migration polymerisation of triethoxyglycidylpropylsilane in the presence of bishydroxymethylcarborane showed[46] that in the first stage of the polymerisation the epoxy-groups interact with the hydroxy-groups of the carborane with formation of a linear polymer in accordance with the following scheme:



In the second polymerisation stage, where the content of epoxy-groups reaches a minimum, the ethoxy-groups are alcoholysed, the product changing from a viscous liquid to an elastic form.

In the absence of compounds with active hydrogen (amines, alcohols, etc.), the siloxane moiety of epoxy-organosilanes can undergo a rearrangement catalysed by alkali without the opening of the oxiran ring[17]. Alkoxysilyl groups can also be hydrolysed under mild conditions without the involvement of the epoxy-component of the molecule[17,26].

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Topochemistry of the Thermal Decomposition of Solid Substances

V.V.Boldyrev

Factors which determine localisation and autolocalisation in topochemical processes are considered systematically in this review. The specific features of the formation and growth of nuclei in topochemical reactions, the role of the anisotropy of the properties of the initial crystal, and various versions of the catalysis of solid and gaseous products during the thermal decomposition of solid inorganic substances are given. Promising investigations in this region are noted. Bibliography of 83 references.

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I. LOCALISATION AND AUTOLOCALISATION OF TOPOCHEMICAL PROCESSES

A characteristic feature of many solid-state chemical reactions is their localisation in definite parts of the crystal. This distinguishes solid-state reactions from those in liquids and gases, the reaction zone in which is uniformly distributed throughout the entire volume.

The localisation of chemical reactions in the solid state, owing to which these reactions have been termed topochemical (from the Greek word "topos", meaning place) is apparent both in the reaction starting at individual points of the solid body which are characterised by increased reactivity and are usually found at the surface, and in that having started at a definite site of the crystal the reaction proceeds by advancement of the reaction zone from the centre at which the reaction started into the neighbouring regions of the crystal. Such a unique nature of the development of topochemical reactions leads in their kinetic analysis to the necessity of considering the process not only in time coordinates (as is done in ordinary chemical kinetics) but also in spatial coordinates. Although this feature of topochemical reactions is well known and one of the main problems of the kinetic analysis of solid-state chemical reactions is the finding of the relation between the rate of formation of the nuclei of the new phase and their growth rate, the physicochemical causes which lead to the localisation of the process have in many instances not yet been studied. In the investigation of specific topochemical reactions it is usually difficult to state beforehand how the initial centres in a solid will be distributed and which factors will be responsible for the occurrence of a process in which the reaction, having started in some part of the crystal, continues to develop in the same place or its immediate surroundings. Moreover, the development of investigations in this direction is important, since it allows both the planning of new methods of directed regulation of the rate of reaction in a solid phase and also the obtaining of a solid decomposition product with previously specified morphological properties.

To the first approximation two groups of factors can be distinguished on which the degree and nature of the localisation process in topochemical reactions can depend. The first group includes those which depend on the potential conditions which exist in the solid until the start of the reaction. These factors are determined by the difference between the reactivities of the various parts of the initial solid substance. They include primarily the difference between the properties of the surface of the solid and

those of its bulk, the non-equivalence of the reactivity of different points of the surface and the bulk of the crystal, associated with the presence of defects of the crystal and defects of the crystal lattice, which determine the mobility of the lattice elements, etc.

The influence exerted by these factors on the reactivity of solids has been examined in detail in many papers concerned with the correlation between the real structure of a crystal and the kinetics of solid-state chemical reactions[1-4]. These questions will not therefore be discussed in the present review.

The second group comprises the factors which determine the change in the degree of localisation during the course of the process. In other words, this group of factors includes those which determine the probability that when the process has started at some point on the surface of the crystal or in its bulk it will continue to develop at the same place or close to it.

In comparison with the factors which belong to the first group, those which are due to the change in the degree of localisation during the course of the process, usually autolocalisation, have been studied much less, although the need for investigations to be made in this direction was stated long ago, starting with the earliest papers dealing with the study of topochemical reactions[5-8].

Not only have the reasons for the autolocalisation of the topochemical reactions been little studied, but in many instances the criteria which characterise the change in the degree of localisation with time remain obscure. Presumably the autolocalisation process, which leads to the formation of nuclei and their growth, is a function of the ratio of the rate constant for the formation of the nuclei to the rate constant for their growth. However, such a determination can hardly be regarded as sufficient and complete, since it is based on an extremely primitive model of topochemical reactions and does not take into account other forms of the autolocalisation process (for example, the change in the degree of "compactness" in the distribution of nuclei in the solid body).

In addition, it remains unknown whether there is a reason for the difference in the nuclei formation and growth constants, that is, that in one instance the development of a reaction proceeds by the growth of a small number of reaction nuclei and in another the reaction develops mainly by nuclei formation. There have been many hypotheses and conjectures along these lines. The most general was advanced by Sakovich[9], in which the change in the degree of localisation of the process was determined as a function of the ratio of "crystal-chemical" and "thermal" components of the activation. The "thermal" component of the activation in the thermolysis of solids is determined by the change in the energy distribution of the phonons in the lattice of the solid and should generally be assigned to the entire volume of the crystal. The "crystal-chemical" component of the activation is the consequence of the breakdown of that equilibrium which existed until the occurrence of a chemical act between the structural units (molecules, atoms, or ions) situated in the bulk of the crystal and the associated change in the reactivity of the structural units adjacent to the lattice node at which the reaction has just taken place. Hence when the thermal component of the activation predominates during the thermolysis, then according to Sakovich it should be delocalised and the reaction must be expected to proceed throughout the entire volume. When the crystal-chemical component of activation predominates an autolocalisation process and its development by the formation and growth of nuclei must be expected.

Despite the obvious merit of Sakovich's scheme, it needs further additions and development. Above all, the hypothesis about the equilibrium distribution in the crystal of the "thermal" constituent of activation is really quite approximate, and as we have already noted[10] the function which corresponds to it should be modelled with allowance for the distribution in the crystal of various types of defects. In addition the crystal-chemical component of activation can also have the most diverse nature and for each specific instance its physical significance should be defined precisely and the factors which could be the cause of autolocalisation found.

II. CAUSES OF THE AUTOLOCALISATION PROCESS IN THE THERMAL DECOMPOSITION OF SOLID SUBSTANCES

The causes of the autolocalisation process in the thermal decomposition can be most diverse. As a first approximation they can be divided into three groups: (a) autolocalisation of thermal decomposition due to crystal-chemical features of the structure of the crystals of the initial substance; (b) autolocalisation of the process due to release of a product during the course of the reaction; (c) autolocalisation of the process, the reason for which is a change in the reactivity of the initial solid substance due to the gaseous products released during the reaction.

We will examine these reasons in more detail.

1. AUTOLOCALISATION OF THE PROCESS OF THERMAL DECOMPOSITION DUE TO CRYSTAL-CHEMICAL FEATURES OF THE STRUCTURE OF THE INITIAL SOLID SUBSTANCE

One of the reasons for the autolocalisation of topochemical processes in general, and of thermal decomposition reactions in particular, can be connected with the anisotropy of the crystal. Thanks to this faces which exhibit increased reactivity can develop during the process. Buntin[7] was interested in the possibility of an autolocalisation of this type during the occurrence of topochemical reactions. This type of autolocalisation has been examined in greater detail in Pavlyuchenko's studies[11,12]. Different places on the surface of a crystal are known to be non-equivalent in reactivity. For example, if the crystal is a cube the particles situated at its vertices are more reactive in thermal decomposition than those situated on the edges. In turn, the particles situated on the edges are more active than those on the faces of the crystal, etc.

We will assume that the reaction starts at the most active sites in the crystal—its vertices. When as a result of the first reaction act a particle is removed from a vertex of the crystal, this brings about the appearance of three new particles which are equivalent in reactivity to that which has disappeared. When these three particles are also removed as a result of chemical reaction, there are then six such particles in the next layer, and so forth (Fig. 1). Since the reactivity of these particles is higher than that of the particles situated in the remaining parts of the crystal the localisation of the thermal decomposition takes place at this particular site.

Hence the mechanism of thermal decomposition is regarded as analogous to that previously developed in studies of the mechanism of dissolution of ionic crystals[13-15]. Therefore, just as in the dissolution of a crystal, as a result of the merging of reaction zones, which

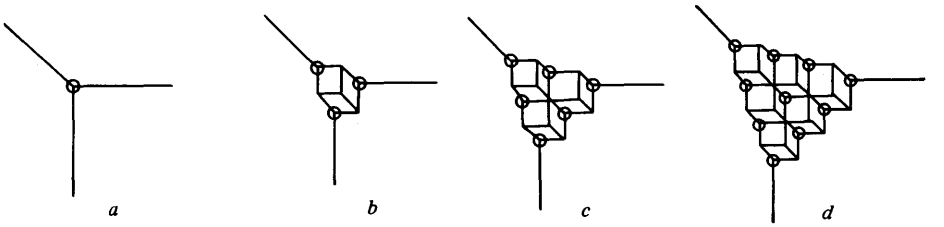


Figure 1. Autolocalisation of the thermal decomposition due to crystal-chemical features of the structure of the initial substance. *a*) Start of the reaction; *b*), *c*), and *d*) separate stages in its development.

are sometimes characterised as a form of negative crystals[16], the crystal ultimately acquires a spheroidal form and the further development of the process is described by the law of contracting spheres.

Thermal decomposition with such a process of autolocalisation is usually characterised by the absence of catalysts among the solid and gaseous products which are formed in the thermal decomposition.

The thermolysis of mercury(II) oxide crystals[16] can serve as an example of this type of process. The decomposition of mercury(II) oxide crystals was found to start at the defect sites on the surface of the crystal and to develop with different rates in different crystallographic directions with the formation of decomposition figures analogous to etch figures and negative crystals. In later studies[17] it was shown that when the temperature was raised the decomposition proceeded over the entire surface. An analogous picture is observed in the thermal decomposition of silver cyanamide[18,19] and in the sublimation of certain ammonium salts, for example, ammonium perchlorate[20]. For the latter it has been shown that when the decomposition (sublimation) takes place at low temperatures the reaction is localised in the zone of dislocations.

2. AUTOLOCALISATION OF THERMAL DECOMPOSITION DUE TO THE FORMATION OF A SOLID PRODUCT DURING THE COURSE OF THE REACTION (AUTOCATALYSIS BY A SOLID PRODUCT OF THE REACTION)

a. General Positions of the Theory of Phase Transformations

The possibility of the autolocalisation of the process of thermal decomposition due to the formation of a solid product during the reaction has been discussed repeatedly[5,8,21,22]. This has been thought[6] to follow from the analogy between the occurrence of topochemical processes and other types of phase transformation (for example, crystallisation from aqueous solutions or from melts, polymorphic transformations, etc.). And although later investigations have shown that this analogy is by no means always complete we will employ it in the present review, mentioning as we go those factors specific for solid-state chemical reactions, which must be taken into account in studying this type of phase transformation.

As follows from the general theory of phase transformations[23-25], the formation of nuclei of a new phase can be regarded as the result of local fluctuations in temperature or concentration in the system, due to which nuclei of a new phase are formed. The change in free energy (the magnitude of which ultimately determines the formation of a new phase) can be written as a sum:

$$\Delta g = \Delta g_v + \Delta g_s,$$

where Δg_v is the change in free energy due to the chemical reaction pertaining to the entire volume, and Δg_S the change in free energy due to the formation of the surface of the new phase.

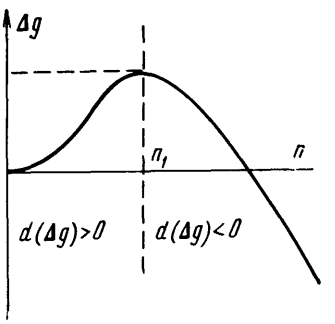


Figure 2. Change in free energy in the formation of nuclei of a new phase during the course of a phase transformation.

The change in free energy for the processes of condensation of vapour and crystallisation from a liquid medium can be written:

$$\Delta g = n(\mu_1 - \mu_2) + \alpha\gamma n^{2/3},$$

where n is the number of moles of reaction product, μ_1 and μ_2 are the chemical potentials of the initial substance and reaction product, α is a coefficient which depends upon the form of the nuclei, and γ the surface energy.

When the solution is supersaturated, $\mu_2 > \mu_1$, the first term in the right-hand part of the equation has a minus sign, and therefore Δg in the change of dimensions of the nuclei is characterised by some extremal value, after reaching which the nuclei become capable of stable growth (Fig. 2).

For the nuclei to reach a dimension greater than the critical one it is necessary to expend energy not only in its formation (Δg) but also the additional amount of energy necessary for the transfer of the particles of the new

phase from the solution or melt through the phase separation boundary. Therefore the rate of formation of the nuclei can be described by the equation:

$$w = c \cdot e^{-\frac{(\Delta g + u)}{kT}}$$

For certain types of phase transformation, for example, in crystallisation from a melt or in the polymorphic change from a high-temperature form into a low-temperature one, the changes $-\Delta u/kT$ and $-\Delta g/kT$ proceed differently (the change in Δg proceeds antibathically to the change in Δu) and as a result a maximum appears on the rate curves—supersaturation. For certain other phase transformations, in particular, in thermal decomposition, this antibathic relation and consequently the maximum may not exist[26].

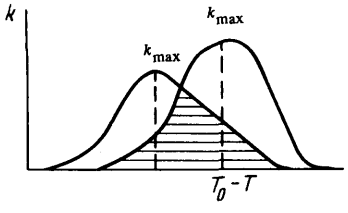


Figure 3. Temperature dependence of the constants for the formation of nuclei and for their growth.

The growth of a nucleus after it has been formed and reached critical dimensions can be regarded as the result of the formation of two-dimensional nuclei on the crystal surface. The change in free energy for the formation of two-dimensional nuclei can be written as

$$\Delta g_2 = n(\mu_1 - \mu_2) + \gamma n^{1/2}$$

and the rate:

$$w = c_2 \cdot e^{-\frac{(u_2 + \Delta g_2)}{kT}},$$

passes through a maximum, just as does the rate for three-dimensional nuclei. Since the dependence of Δg_1 and Δg_2 on supersaturation is different, u_1 and u_2 are different, and so are c_1 and c_2; in general, the positions of these maxima do not coincide (Fig. 3) and therefore either the formation or the growth of nuclei, or both processes together, can take place, depending upon the supersaturation in the system (shown on the Figure by the departure of the temperature from the equilibrium value in crystallisation, induced by cooling of the system).

b. Phase Transformations in the Thermal Decomposition of Solid Substances

When this theory is used for other types of phase transformation, and, in particular, for thermal decomposition, allowance must be made for those specific factors which can significantly alter the general picture of the transformation.

Formation of clusters. Topotaxy. An important factor, which determines both the relation of the chemical and phase stages and also the general nature of the influence exerted by the nuclei of the reaction product on the properties of the initial crystal is the presence of a coherent bond between the lattices of the initial substance and the reaction product.

The possibility of the appearance of this factor depends, firstly, upon some specific features of the formation of nuclei of a new phase in the occurrence of solid-phase processes, and secondly, upon the possibility of effecting an approximate correspondence between the lattice of the initial substance and the lattice of the product.

By analogy with the processes which take place in crystallisation from a melt or a solution when the heterophase fluctuations are the result of the motions of individual atoms or molecules, nuclei are also formed when processes occur in the solid phase. However, the results of more detailed investigations showed that in fact the formation of nuclei in solid-phase reactions is a more complex process, which includes the stage of aggregation in clusters of point defects or dissolved atoms, which become especially significant at the moment of the transformation preceding the formation of a nucleus of the new phase. The interaction can be different in nature but also appears for monotypical defects and for defects of different types.

For identical defects (or atoms) in a polar crystal it comprises the forces of repulsion due to the interaction of the coulombic field and the field of the elastic stresses which surround the defects in the crystal and the attractive forces due to the quantum-chemical interaction. When the attractive forces are greater than the repulsive forces the curves of the potential energy of interaction will be characterised by a minimum. When the depth of this minimum is greater than the mean energy of the phonons in the lattice (κT) the defects can be expected to form clusters[27,28].

For defects of different signs the possibilities of interaction are increased to an even greater degree, for both elastic and coulombic interaction in this instance can lead to attraction and the probability of the formation of clusters is increased accordingly.

In this sense the dependence of cluster formation and in particular of the structure of the clusters in the very first stages on the conditions under which separation of the new phase takes place is extremely important, although there is almost no information about this. Among the few papers in this direction is that of Johanneson and Person[29], who used an electronic computer to model the growth of atomic clusters in the deposition of thin films of silver on the surface of alkali halide crystals. For the modelling they took a relatively simple model, in which the interaction between the adsorbed silver atoms was given by the Morse function

$$\Phi(r) = D[\exp -2\alpha(r - r_0) - 2\ \exp -\alpha(r - r_0)],$$

the calculated values of which for silver are known, the interaction between the adsorbed atoms and the surface is given by the potential function:

$$V(x, y, z) = -\left[Q_d/4\left(\sin\frac{2\pi x}{x_0} + n\frac{2\pi y}{y_0}\right) + Q_{ads} - Q_{dif}/2\right]\exp(-z/z_0)$$

where x_0, y_0, and z_0 are the lattice constants in the direction of the three geometric axes, and Q_{dif} and Q_{ads} are the activation energies of the diffusion and adsorption of the atoms on the surface.

The variation, as parameters of the system in the determination of the energy minimum, of Q_{ads}, Q_{diff}, and d (periodicity of the lattice) showed that not only two-dimensional but also three-dimensional, nuclei can be stable, and that of the three parameters being varied the most important is the interatomic distance of the lattice (d), on which the adsorption takes place. It has been shown[29] that as a result of the change in d the form of the primary cluster consisting of six atoms changes from rectangular to orthorhombic. The form of the cluster is also extremely sensitive to the number of atoms forming the cluster and its dimensionality. What is significant in this is that the three-dimensional nuclei-clusters can be just as stable as the two-dimensional and the addition of each new atom, at least in the initial stage, significantly affects the form of the cluster.

It is quite natural that a similar type of estimation can also be made when we are considering not the deposition of metal atoms from the gas phase on the surface of a crystal, but a solid-phase reaction in which clusters are formed from the defects, for example, from internodal ions, ionic vacancies, and not in a vacuum, but within the crystal lattice. The number of parameters being varied in this instance should be changed and the value of the Morse function should be found for the interaction of the internodal ions, vacancies, etc. Evidently, in principle the approach used for calculating the form of the clusters in the epitaxial growth of thin films is applicable also for topochemical reactions.

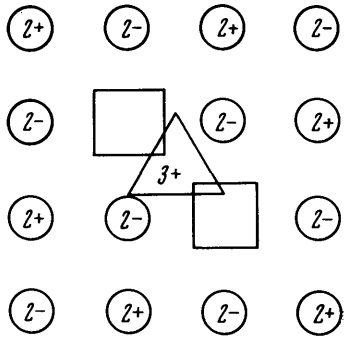


Figure 4. Elementary stages of the formation of Fe_3O_4 in the decomposition of FeO.[28]

As an example, now classical, there is the formation of nuclei of a magnetite phase in the decomposition of wüstite[30]. In the decomposition, which proceeds by the overall scheme:

$$4FeO \rightarrow Fe + Fe_3O_4,$$

the composition of the wüstite phase becomes $Fe_{1-x}O$, where x denotes a position in the lattice occupied by Fe^{3+} ions and cationic vacancies, the formation of which is necessary for the compensation of the charge. Being found at the normal node of the lattice and having smaller dimensions than Fe^{2+}, the Fe^{3+} ion tends to go to an internodal position with the formation of a complex from the Fe^{3+} ion and two cationic vacancies situated symmetrically relative to it. The Fe^{3+} ion occupies the positions which are typical for the tetrahedral node of the spinel formed (Fig. 4). Similar examples are also known for other solid-phase reactions[31].

In addition to the crystal-chemical aspect of the significance of clusters it is also important to bear in mind the thermodynamic aspects[31], which lead to an increase in the probability of the surmounting of the energetic barrier for attaining nuclei of critical dimensions.

An orientation correspondence of the crystal-chemical parameters of the old and new phases is extremely important not only for the formation of these phases but also to an even greater extent for their growth in ensuring that the lattices of the new and old phases are coherent.

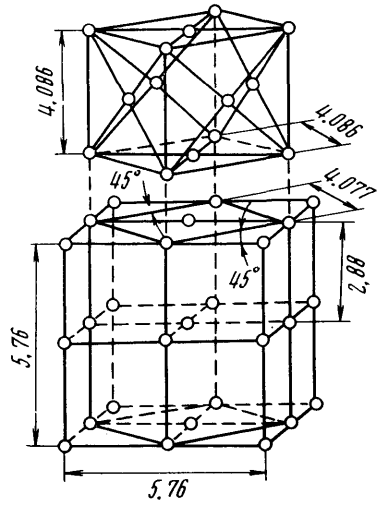


Figure 5. Orientation correspondence between the lattices of silver bromide and silver.

The condition under which there is an orientation correspondence which ensures the uninterrupted change from a phase of the initial substance to a phase of the reaction product was formulated by Dankov[32,33]. According to Dankov, chemical changes on the surface of a solid body develop in such a manner that the configuration of the atoms of the initial phase is retained (or more precisely, almost retained) in the new solid phase. The crystal lattice of the new phase formed in this process is joined with that of the initial phase by similar crystal planes, the parameters of which remain minimal. As an example of the orientation correspondence in decomposition reactions, there is the orientation growth of silver on the surface of silver bromide (Fig. 5). Whether two-dimensional nuclei of a new phase will be orientated according to the lattice of the initial substance or whether independent nuclei will be formed depends on the deformation energy of the two-dimensional lattice of the new phase E and the work of formation of the independent three-dimensional nucleus A. If $E < A$ there will be an orientation correspondence and the epitaxial and topotaxial growth of the nuclei of the new phase will be possible; if $E > A$ then the formation of the nuclei of the new phase will proceed independently of the lattice of the initial substance.

This principle was developed further[34,35], and it was found that when the orientation correspondence is observed the lattice of the product can correspond with the lattice of the initial substance in two (epitaxy) or three (topotaxy) measurements. Many examples of topotaxial transformations in solid-state chemical reactions (including those of thermal decomposition) are now well known and have been reviewed[36,37].

Owing to the topotaxial change from one crystal lattice to another there is always a decrease in the activation energy of transformation, which for non-topotaxial transformations should be equal to or greater than the heat of the phase transformation[38,39].

It is often possible for there to be produced a fine structure of the lattice of the reaction product under the lattice of the initial substance and for topotaxy to be guaranteed not only in the initial part of the process but also in its subsequent stages. This occurs when there is disparity between the lattice parameters of the initial substance and the transformation product, which can increase with growth of the product lattice along the phase separation boundaries, will be removed by the formation of dislocations at the separation boundary of the lattices[40], and especially will ensure retention of continuous contact between the lattice of the initial substance and the reaction product.

Thickness and structure of the interfacial zone. For many processes which take place in the solid phase, including thermal decompositions, the rate of the chemical reaction can be much greater than the rate of the phase stage and therefore the stages will not agree in either time or space. The possibility of the occurrence of topochemical decomposition reactions in this manner was noted by Roginskii[41].

Such processes were studied in detail later by Frost and coworkers[42-44]. Owing to the separation of the chemical and phase stages of the process it appears that an intermediate layer is formed instead of an interfacial surface which separates the lattice of the solid reaction product and the initial substance. Sometimes, when the chemical and phase stages are separate and the localisation of the process at the phase separation boundary is not connected with the catalytic action of the solid product there is almost complete agreement of the activation energy of thermal decomposition with the change in enthalpy during the process. As examples of this type of thermal decomposition, there are the decompositions of silver carbonate[44] ($\Delta H = \Delta E = 20$ kcal mole^{-1}), calcium carbonate ($\Delta H = \Delta E = 50$ kcal mole^{-1}),[45] ($\Delta H = \Delta E = 42.5$ kcal mole^{-1}) and cobalt[46] and zinc sulphates ($\Delta H = \Delta E = 54$ kcal mole^{-1}).

A similar agreement of the activation energy with the change in enthalpy is also observed for other phase transformations in the solid phase (for example, the polymorphic transformations of sulphur, 2-nitroaniline into 3-nitroaniline, etc.[39]), when the possibility of a topotaxial transformation from the initial substance to the reaction product is absent and the formation of the lattice of the new phase precedes the complete breakdown of the initial lattice.

The reasons for the formation of a layer instead of a surface of separation of an initial crystalline phase and a reaction product can be various. On the one hand, as Cahn and Hillard[49] have shown, thermodynamic causes linked with the need for minimising the free energy at the phase separation boundary can lead to the appearance of a layer between the initial substance and the reaction product. According to this condition the minimum free energy at the separation boundary occurs at a strictly definite thickness and composition of the separation boundary, and these ultimately are functions of the temperature and the heat of mixing of the initial substance and reaction product.

On the other hand, after the appearance of the transitional layer which separates the phase of the initial substance and the phase of the product, kinetic factors can also be responsible. Their effect will appear when, for example, the change of the product phase from metastable amorphous or cryptocrystalline into the thermodynamically stable crystalline state is hindered for some reason.

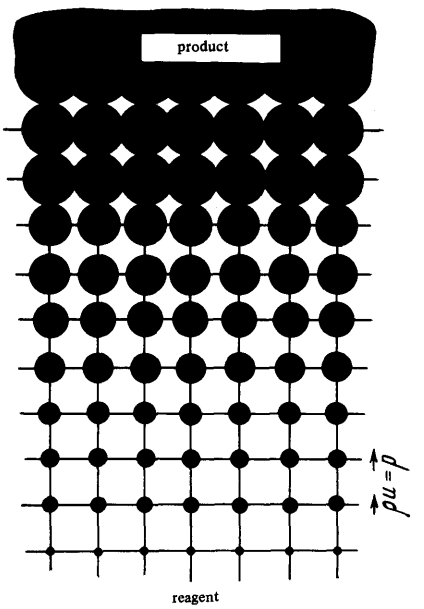


Figure 6. Diffuseness of the reactivity zone at the separation boundary between the initial substance and the reaction product[53].

The possibility of allowing for this factor can be shown by the example of the dehydration of a crystalline hydrates[50,51]. In this thermal decomposition the probability of the separation of chemical and phase stages ultimately is greater the stronger the bonding with one another of the atoms in the dehydration products formed. When this bond is strong enough, as is observed for the products obtained in dehydrating zeolites, the phase stage generally cannot start until after the complete removal of the water. On taking a crystal hydrate in which the structural components in the anhydrous residue are still bonded but much more weakly than in the zeolites (for example, magnesium sulphate heptahydrate) the phase stage will be observed but with some lagging behind the chemical one, and between the lattices of the initial crystal hydrate and of the dehydration product an intermediate amorphous layer is formed.

If we take such a crystal hydrate, in which the energy of the bond between the elements of the lattice is low (for example, copper chloride dihydrate) the chemical and

phase stages can proceed at similar rates and therefore in this instance the thickness of the intermediate layer between the initial substance and the reaction product can be extremely low.

The separation of the chemical and phase stages and the associated conversion of the interfacial surface into a layer can affect the kinetics of the thermal decomposition in various ways. Firstly, the separation of the crystalline phase of the reaction product from the initial substance also reduces the probability of the catalytic action of the reaction product on the initial substance (this will appear particularly when the mechanism of catalysis is connected with the orientation-deformation interaction of the lattices of the initial substance and reaction product). Secondly, the conversion of the planar reaction zone into a layer implies the existence of significant changes in the models which are now used for the kinetic analysis of topochemical reactions (in most of these it is assumed that the interfacial surface is planar).

de Boer[52] was interested in such special instances of the occurrence of topochemical changes. Hill[53,54] showed that the diffusion of the reaction zone (see Fig. 6) and the change from a planar reaction zone to a layer can occur when there is a drift of atoms or ions from the layer of the product into the layer of the initial substance, as a result of which there is continuous formation of nuclei of the new phase around the main reaction front. At a certain ratio of the rates of nuclei formation, the rate of diffusion of ions which "contaminate" the initial substance, and the rate of motion of the interphase surface, a diffusion layer is formed between the initial substance and reaction product; this layer consists of a mixture of the initial substance and nuclei (of various sizes) of the reaction product. The result of this can be many kinetic anomalies, for example, the anomalously high values of the pre-exponential factor in the dehydration of chromium alum, observed by Anous and coworkers[54].

When the decomposition can proceed not only on the surface of the solid body but also within its bulk and the diffusion coefficient of the volatile product which is formed is sufficiently great the situation can arise in which a diffusion layer is also formed instead of a smooth separation surface. It is easy to understand that the profile of the gradient of the concentration of the reaction product removable from the system will be the reverse of that examined by Hill. A diffusion-kinetic model of such reactions was recently given by Mandelis and Strunin[55].

Deformation of the lattice close to a growing nucleus. In the formation of crystals of a new phase from a gas, solution, or melt, the volume changes are readily compensated as a result of flow of the liquid or gas. When the initial substance is a crystal then the relaxation of the deformations which occurs during the course of the transformation can be effected either by elastic deformation or plastic flow, or alternatively by diffusion processes[56]. Therefore the equation for the free energy of nuclei formation for solid-phase processes contains yet another term Δg_e connected with the deformation of the surrounding medium by the growing nucleus:

$$\Delta g = \Delta g_v + \Delta g_s + \Delta g_e$$

The second term Δg_S for solid-phase processes also has a somewhat different physical significance, since instead of the surface energy it includes the energy of the surface of separation between the two crystalline phases.

Usually this energy is represented as the sum of chemical and structural constituents[57]. The chemical constituent can be found when the crystal structures of the initial phase (α) and the reaction product (β) have the same symmetry and lattice parameters. In this instance the surface energy at the $\alpha-\beta$ phase separation boundary can be evaluated simply to the first approximation as the energy of interaction of nearest neighbours:

$$\sigma_{\alpha\beta} = n_s z_s [\varepsilon_{\alpha\beta} - {}^1/_2(\varepsilon_{\alpha\alpha} + \varepsilon_{\beta\beta})],$$

where n_S is the number of atoms per unit area of the interfacial surface, z_S the number of $\alpha-\beta$ bonds per α or β atom in the plane of the $\alpha-\beta$ phase boundary; and $\alpha\beta$, $\alpha\alpha$, and $\beta\beta$ are the energies of the bonds between the different types of atoms in the system at 0°K. Since these energies are difficult to determine directly, the formula for calculating the energy of dissolution ΔE per g-mole or g-phase of β in an infinitely dilute solution of α and β can be used for the experimental determination of $\sigma_{\alpha\beta}$:

$$\Delta E = NZ_1[\varepsilon_{\alpha\beta} - {}^1/_2(\varepsilon_{\alpha\alpha} + \varepsilon_{\beta\beta})],$$

where N is Avogadro's number and Z_1 the coordination number. On combining these equations, we have:

$$\sigma_{\alpha\beta} = \frac{n_z \cdot Z}{NZ_1}\Delta E$$

To calculate the structural constituent, we assume that the lattice parameters of phases α and β at the phase separation surface are different although the arrangement of the atoms in the two lattices are similar. Then the parameter of non-correspondence of the lattices (maladjustment) is determined as:

$$\Delta = (a_\alpha - a_\beta)/a_\alpha,$$

where a_α and a_β are the atomic distances in the regions in contact. Since the density of dislocation is proportional to $1/\Delta$, then knowing the energy necessary for the formation of a single dislocation the structural constituent can also be calculated. $\sigma_{\alpha\beta}$ can also be approximately represented as the difference in energy of the lattices of the phases in contact per unit interfacial surface[58].

The deformation of the lattice both owing to the energy at the phase boundary and owing to the difference in molecular volumes of the initial substance and reaction product can be calculated when the volume change, the form of the region in which the change took place, and the form of the crystal of the new phase are known (the possibility of such a calculation has been shown for certain examples of phase changes in metals and alloys[56]).

According to Nabarro's work[59], the form of the nuclei which are formed should depend mainly upon the two main components bringing about the deformation of the lattice which surrounds the growing nucleus: the components of the deformation K_S, associated with the interfacial energy, and the components of dilatation K_V due to the change in volume during the transformation. When K_S is large, the nuclei will tend to adopt the form with the minimal ratio between the surface and the volume, that is, when the medium in which its growth takes place is isotropic, the form of a sphere. When K_V is large, the tendency to the minimisation of the energy of deformation will result in the nuclei formed being planar and extended along the surface. The combination of these factors with the anisotropy of the deformability of the initial substance will lead to various forms of nuclei, which are observed in experimental investigations.

The deformation of the lattice of the initial crystal as the nuclei of a new phase grow in it has been observed

experimentally in certain instances, for example, by Morrison and Nakayama[60], who studied the topochemical interaction of gaseous chlorine with a potassium bromide crystal and used birefringence for observing the deformation of the bromide crystal around the growing nucleus. As Fig. 7 shows, there is especially pronounced deformation in the region of the crystal adjacent to the corners of the growing nucleus.



Figure 7. Formation of a deformation zone around the growing nucleus.

The deformation of the lattice around a nucleus can lead to a change in the reactivity of the crystal in this region. The low-temperature transformation of austenite into martensite is the classical example of how significant is the elastic deformation of the lattice close to the growing nucleus for the development of solid-state processes[61]. The peculiarity of this process is that the transformation of the initial substance (austenite) into martensite proceeds without diffusion and for it to occur only requires some movement of the iron atoms in the lattice by a distance less than the parameters of the lattice (Fig. 8). The elastic stresses which arise in austenite as a result of the appearance of the nuclei of a new phase and which are situated in advance of the phase transformation front help the transformation to become collective and the rate of transformation to become very large, approaching the rate of propagation of sound in austenite.

Dislocations evidently may occur as a result of the relaxation of lattice deformations in the region around growing nuclei. This is confirmed by the experimental results on the increase in the density of dislocations close to the growing nucleus, which have been obtained for several systems[62-64].

The formation of dislocations in a crystal close to a growing nucleus can significantly alter the reactivity in this place, particularly when the decomposition takes place at low temperatures. In a thermal decomposition the formation of dislocations simultaneously alters both the conditions of transport of the reagents and reaction products in the mass of the crystal and also has an action on the decomposition of the solid solution and reconstruction of the lattice of the initial substance, which usually accompanies the thermal decomposition.

Possible paths for the influence of dislocations on the thermal decomposition have been examined frequently. It has been thought that in the thermolysis of certain ionic crystals, for example, lead azide and sodium bromate at very low temperatures, the dislocations will be the only places in the crystal where it is possible to expect development of a reaction[65]. The dislocations can be channels through which rapid migration of the product ions can occur, from the "contaminated" non-reacted region of the initial crystal, according to Hill's hypothesis, which we have already mentioned. The appearance of channels by which ions can move at rates many times greater (this difference can reach several orders of magnitude) than in the bulk of the crystal enables dislocations to play a significant part in the supply of material needed for the construction of the lattice of the reaction product. This is necessary to ensure the normal growth of the nuclei for the thermal decompositions in which the stoichiometry of the nuclei growth process proceeds owing to one of the elements of the lattice and the aggregation of these atoms or ions is a necessary stage. For example, such happens in the thermal decomposition of metal salts to the metal (for example, in the thermolysis of silver oxalate).

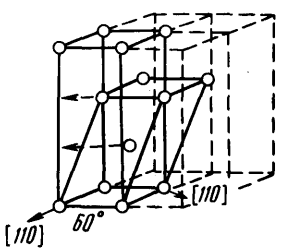


Figure 8. Scheme of the martensitic transformation.

In addition to the influence on the transfer process of dislocations which arise as a result of the relaxation of elastic strains in the lattice of the initial substance around the growing nucleus, the thermal decomposition can be accelerated by impurities and dissolved atoms and ions from the lattice accumulating in the zone of extension of the dislocations. Since in this part the most favourable conditions for the breakdown of the solid solutions and reconstruction of the lattice are set up, the place where the dislocations emerge at the surface are often potential centres at which formation of the nuclei of a new phase occurs during thermal decomposition. The change in the topography of the position and density of the dislocations in the crystal (for example, owing to polygonisation in annealing and the physical ageing of the crystals) is reflected in the kinetics of the thermal decomposition.

An illustration of what has been said is given by the results of our experiments, which showed a connection between the change in the density of the dislocations in crystals of lead oxalate and the kinetic parameters of the thermal decomposition of this salt (cf. Ref. 66 and pp. 124–157 of Ref. 1) and also the work of Thomas which was specially concerned with the appearance of dislocations in various topochemical reactions[67-71].

c. Other Forms of Autolocalisation Process Connected with the Influence of a Solid Reaction Product

In addition to the deformation action associated with the orientation interaction at the separation boundary of two phases and the volume changes throughout the process in certain types of topochemical transformations of a solid reaction product there are other specific influences on the reaction rate. When the thermal decomposition is a redox reaction the solid product which is formed can alter the conditions under which an electronic transition takes place and thereby accelerate or inhibit the thermal decomposition.

As an example of such an effect, which arises in the formation of a solid product, we can examine the development of the thermal decomposition of barium azides. According to the ideas of Torkar and his coworkers[72,73] the formation of nuclei in the thermolysis of barium azide takes place as a result of the capture of the excited state of the azide ion on a defect, which can, for example, be an anionic vacancy. Owing to this, as a result of the transfer of an electron trap

$$N_3 + \text{phonon} \rightleftarrows N_3^{-*} + \square \rightleftarrows [\square N_3^{-*}],$$
$$[\square N_3^{-*}] \rightarrow [\square e]\, N_3^0,$$

and then its localisation on a neighbour with a cation trap, formation of a Ba^+ ion takes place:

$$[\square e]\, N_3^0 + Ba^{2+} \rightarrow [\square Ba^+]\, N_3,$$
$$2N_3^0 \rightarrow 3N_2,$$

and the azide radical is converted into nitrogen. It is assumed that the complexes

$$[\square e\, Ba^{2+}] \rightleftarrows [\square Ba^+]$$

are nuclei of the last thermal decomposition. Since the Ba^+ level should represent an acceptor level in the lattice lying at the limits of the forbidden band, its presence will facilitate the last transfer of an electron from a neighbouring azide ion at this level:

$$\square_a Ba^+ + N_3^- \rightarrow \square_a\, BaN_3^0 \rightarrow \square_a Ba\square_a + {}^3/_2\, N_2,$$

as a result of which a complex is formed from a metal atom and two anionic vacancies:

$$\square_a Ba\square_a + Ba^{2+} \rightarrow [\square_a BaBa\square_a]^{2+} \rightarrow \square_a Ba^+ Ba^+ \square_a$$

As a result of the process, stabilisation of the complex and regeneration of its acceptor properties takes place (Fig. 9). This ensures maintenance of the conditions for the autolocalisation of the process at the place where the nucleus arises and determines its growth. Since the conversion of barium azide into the metal proceeds topotaxially and diffusion processes do not play a significant part, the limiting rate of growth of the stages is the redox process at the metallic barium—azide boundary. The nature of the development of the process described above corresponds to activation energies of formation (63 ± 5 kcal mole^{-1}) and growth (26 ± 1 kcal mole^{-1}) of nuclei of metallic barium in the thermolysis of the azide.

If the solid substance which undergoes thermal decomposition is an electron or hole semiconductor and the reaction for the decomposition is a redox reaction then the solid product which is formed in the decomposition can alter the reactivity of the substance in the region adjacent to the place where formation of the reaction product occurred, owing to the changes in the concentrations of electrons and holes close to the phase boundary. An example of this process is the thermolysis of potassium permanganate, the mechanism of the decomposition of which was studied in detail in our laboratories[74]. According to the scheme proposed, the thermal decomposition of potassium permanganate, which is an n-type semiconductor[75,76] takes place owing to the transfer of an electron from one permanganate ion to another:

$$MnO_4^- + MnO_4^- \underset{k_2}{\overset{k_1}{\rightleftarrows}} MnO_4^0 + MnO_4^{2-}$$
$$\downarrow$$
$$MnO_2 + O_2$$

As a result of the transfer the unstable MnO_4^0 is formed, which immediately decomposes into MnO_4 and O_2. On making the natural assumption that the electronic decomposition is rapid and the rate-limiting stage is the decomposition of the MnO_4^0 radicals then a stationary state is established in the system.

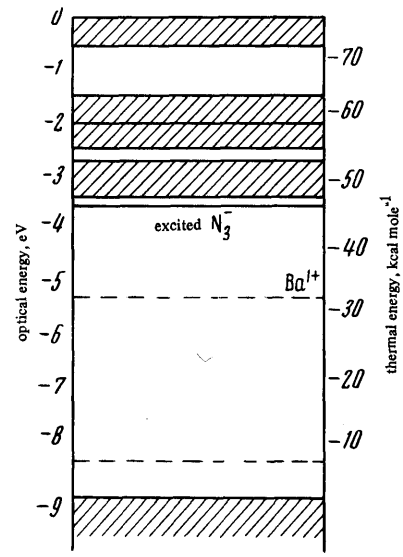


Figure 9. Scheme of the energy levels in barium azide.

It is easy to see that the overall rate of the process will be increased by the shift of the electron—hole equilibrium k_1/k_2 to the right and decreased when it is shifted to the left. The condition for such a shift in the equilibrium can arise, for example, owing to the contact potential difference at the separation boundary between the initial permanganate—and the solid reaction products, which are MnO_2 and the double salt $K_3(MnO_4)_2$, which is an ion associated with the MnO_4^{2-} ion.

Measurement of the electron work functions of potassium permanganate, manganate (as the double salt), and manganese dioxide showed (Fig. 10) that under conditions close to those for thermal decomposition the electron work function of manganese dioxide is greater than that for permanganate, but that from manganate, on the other hand, is less. In accordance with this and our scheme of thermolysis of permanganate, MnO_2 should be an acceptor of electrons and therefore should catalyse the thermal decomposition of permanganate, whereas manganate should be a donor of electrons and inhibit thermolysis. Actually, as is clear from the results (Fig. 11) on the thermolysis of potassium permanganate with additions, the addition of

MnO_2 accelerates the thermal decomposition of permanganate, but additions of manganate, on the other hand, retard it. Therefore the well-known phenomenon of autocatalysis in the thermal decomposition of permanganate is itself the superimposition of the catalytic action of one of the reaction products and the inhibiting action of the other.

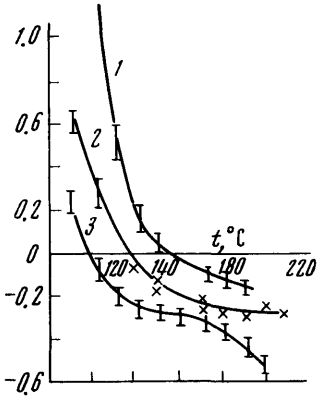


Figure 10. Work function from permanganate and its decomposition products: *1*) $K_3(MnO_4)_2$; *2*) $KMnO_4$; *3*) MnO_2.

A peculiarity of the autolocalisation in this instance is that the influence of the solid product of the reaction is not limited to the surface layer of the initial substance adjacent to the product but extends into the depth of the initial solid phase according to the length of the screening charge and therefore the formation of MnO_4^0 radicals can take place in the bulk of the crystal at some distance from its surface. Since the decomposition into MnO_2 and O_2 is almost irreversible, the liberation of gas in the bulk of the crystal ultimately leads to the dispersion of the crystal during its thermal decomposition. This and not the difference in the lattice parameters of the product and the initial substance, which, judging from our results, will hardly be significant, is the true reason for the self-shattering of permanganate.

In addition to what has been described, there can be other forms of autolocalisation of a process, for example, those linked with special conditions for proton transfer, which exist at the phase separation boundary in the dehydration of crystal hydrates and oxide hydrates, the presence in this place of anomalous valence states of the elements, etc.[77,78] However, these factors have been insufficiently studied.

The following conclusions can be drawn on the basis of the above considerations: the influence of the reaction product depends very strongly on the degree of its contact with the initial substance. Therefore to the first approximation all the thermal decompositions can be divided into two classes, depending upon whether the coherency of the lattices of the product and initial substance during the course of the process are maintained or not. It is quite natural that the coherency, and consequently the contact, will be ensured to the greatest extent when the formation of a product from the initial substance takes place topotaxially. However, here only some of the properties will be altered by the discontinuity at the separation boundary. For example, in the thermal decomposition of barium azide, the lattice parameter changes smoothly at the separation boundary but the electrical properties change suddenly. With growth in the layer of reaction product the necessary orientation correspondence can be ensured by the substructure of the lattice of the product under the lattice of the initial substance (or the reverse), for example, owing to the formation of dislocations at the phase separation boundary.

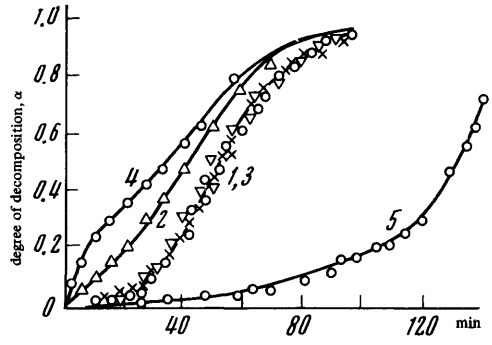
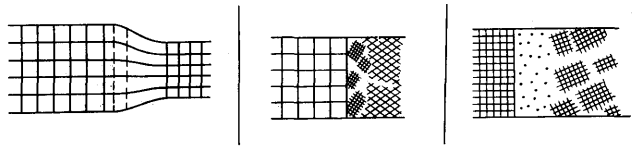


Figure 11. Kinetic curves of the influence of MnO_2 and K_2MnO_4 on the decomposition of $KMnO_4$. *1*) Decomposition of permanganate at 220°C; with addition of MnO_2 (reagent); *2*) the same with addition of MnO_2, obtained in the thermal decomposition of $KMnO_4$; *3*) with addition of MnO_2 obtained by heating $Mn(NO_3)_2$ at 170°C; *4*) with addition of MnO_2 made by oxidation of 5% $MnSO_4$ heated to 60°C; *5*) with addition of K_2MnO_4 (cocrystallised); *6*) decomposition of permanganate without any additions (below *1*, *3*).

Table 1.

Nature of the formation of a solid reaction product

coherent (topotaxy)		incoherent	
total	partial	$V_{phase} \sim V_{chem}$	$V_{phase} \ll V_{chem}$



Factors leading to a change in the reactivity of a solid substance close to incipient nuclei of the product

(a) deformation connected with energy of interfacial orientation interaction of the two lattices; (b) deformation connected with change in volume; (c) change in the conditions for the occurrence of electronic and ionic processes in the near-contact region at the phase separation boundary.	(a) deformation connected with the change in volume; (b) change in the conditions for the occurrence of electronic and ionic processes in the near-contact region.	(a) change in the conditions for the occurrence of electronic and ionic processes in the near-contact region.

Another extreme instance is the complete destruction of the lattice of the initial substance as a result of the thermal decomposition and absence of coherency between the lattices of the initial substance and the reaction product. In this instance, depending upon the ratio of the

rates of the chemical and phase stages observable as a result of the reaction of the amorphised layer, the product can either be found in contact with the initial substance or will be separated from it by a layer of the amorphous material: depending upon which of these two distinct possibilities arises so will the influence of the solid product of the reaction on its rate be determined (Table 1).

If there is a coherency between the lattice of the product and the lattice of the initial substance it is to be expected that the energy of interfacial interaction will greatly affect the properties of the initial substance. When as a result of the reaction there is a considerable increase in the specific volume of the reaction product in comparison with the volume of the initial substance, there can prove to be a significant associated deformation of the lattice of the initial substance, which will happen even in the absence of coherency.

Finally, the change in the nature of the occurrence of electronic and ionic processes in the region near the contact can appear when the phase and chemical stages do not coincide.

3. AUTOLOCALISATION OF THE THERMAL DECOMPOSITION DUE TO THE RELEASE OF GASEOUS PRODUCTS DURING THE COURSE OF THE REACTION (AUTOCATALYSIS BY GASEOUS PRODUCTS)

When the gaseous products formed during the thermal decomposition undergo further chemical change and the resulting products interact with the substance that has not yet reacted, this can also be a reason for the autolocalisation of the thermal decomposition.

An example of this type of autolocalisation is the formation of nuclei in the low-temperature thermal decomposition of ammonium perchlorate. Bircomshaw[79] showed that the low-temperature decomposition of ammonium perchlorate is accompanied by the formation of cigar-shaped nuclei. More detailed microscopical observations showed that each such nucleus is itself an aggregate consisting of finer nuclei and the growth of a nucleus takes place by the appearance of new nuclei around the edges of the aggregate[20]. Since ammonium perchlorate decomposes without the formation of a solid reaction product, the formation of nuclei in the low-temperature thermal decomposition could not be connected with the catalytic influence of the solid reaction product, the nature of the development of the nucleus does not provide the possibility of relating the localisation of the low temperature thermal decomposition with the anisotropy of the properties of the initial crystal. It was therefore postulated that the reason for the autolocalisation process in the low-temperature decomposition of an ammonium perchlorate could be the action, during the course of the process, of gaseous products formed during the course of the reaction (for example, the oxidation of ammonia by the products of the thermal decomposition of perchloric acid from the ammonium perchlorate that has not yet reacted, Fig. 12).

In the investigation of low-temperature thermal decomposition[80] it was shown that in this instance, when the dissociation of ammonium perchlorate takes place on the inner, not the outer, surface of the crystal (for example, at the boundaries of blocks, dislocation nuclei, etc.), since the molecular weights of ammonia and perchloric acid are different, it could be expected that during the course of the process in these parts there will initially be

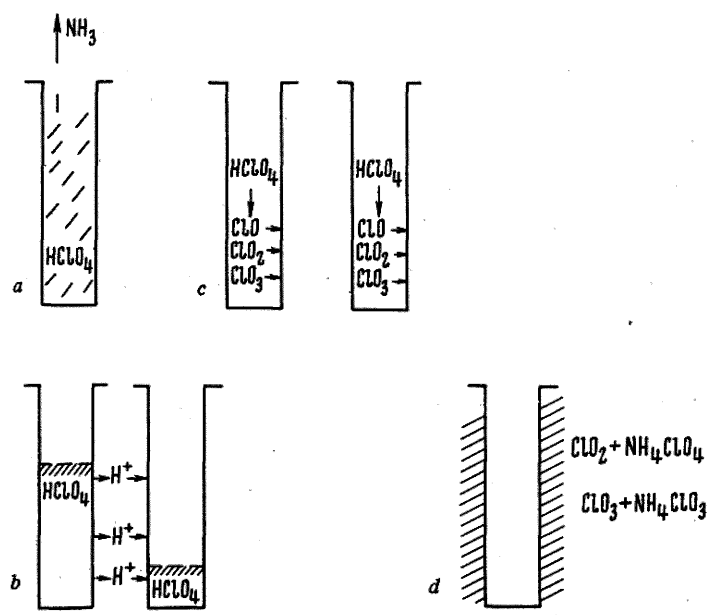
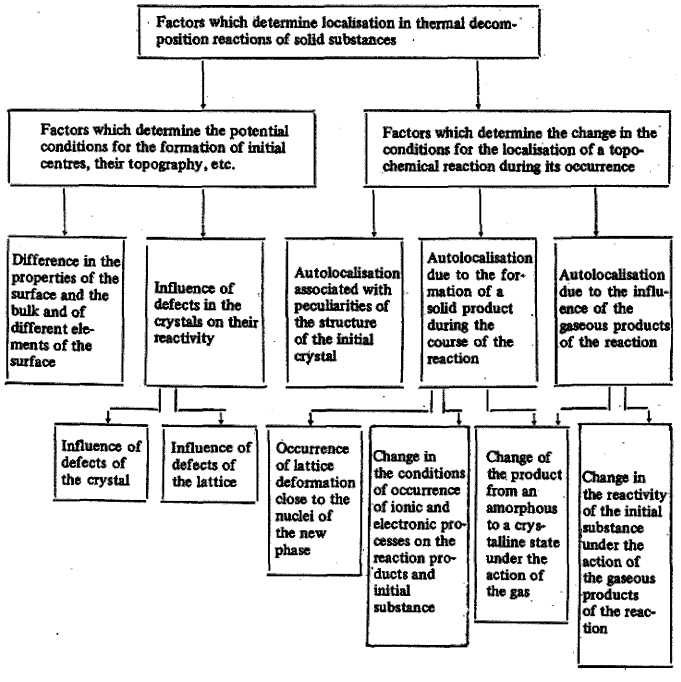


Figure 12. Scheme of low-temperature decomposition of ammonium perchlorate: *a*) separation of ammonia and perchloric acid in a pore due to the difference in the diffusion rates; *b*) migration of perchloric acid into a neighbouring pore; *c*) decomposition of perchloric acid; *d*) interaction of the decomposition products of perchloric acid with unreacted ammonium perchlorate.

an accumulation of perchloric acid and then its decomposition. Simultaneously with the decomposition owing to the proton conductivity[81,83] which is specific for ammonium perchlorate migration of the acid to the neighbouring potential centre (for example, a dislocation nucleus) and the initiation of the reaction in it can occur. The decomposition products of perchloric acid (for example, ClO, ClO_2, and ClO_3) react with ammonium perchlorate on the walls of dislocations of the boundaries of blocks, and subsequently thermal decomposition takes place owing to this reaction. It is extremely significant that during the course of the reaction there can be regeneration of the molecules of perchloric acid or chlorine oxide (for example, according to the scheme of Koroban and Svetlov[83]), which ensures decomposition of the chain, thanks to which the growth of a nucleus, as distinct from its formation, is much less dependent upon the equilibrium pressure of perchloric acid.

Table 2.



Hence whereas the formation of a reaction nucleus is connected with the dislocation processes of ammonium perchlorate and the subsequent decomposition of perchloric acid, the growth of nuclei proceeds due to the interaction of the products of perchloric acid with ammonium perchlorate.

The difference in the chemistry of these processes corresponds to different activation energies—50 ± 5 kcal $mole^{-1}$ for the formation of reaction nuclei and 30 ± 2 kcal $mole^{-1}$ for their growth process. This also is responsible for the experimentally observable autolocalisation process, which continues to develop preferentially at the place where the reaction started.

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Table 2, which we give at the end of the review, shows the mutual relation between the various factors which determine the localisation in the thermal decomposition of solid substances.

The study of the physicochemical reasons responsible for the localisation and autolocalisation of the thermal decomposition is an extremely important task. Its solution allows us to understand more thoroughly the peculiarities of the development of topochemical reactions and to note the path of their directed regulation. Should this problem be solved, then (a) conditions will be created for the quantitative study of the rates of topochemical reactions; (b) new possibilities of regulating the rates of topochemical reactions during their occurrence will be discovered. Until then in most instances the directed regulation is limited by the initial stage of the process and is carried out at the qualitative level.

The experimentally observable autolocalisation process considered above which is recorded by investigators as the ratio between the formation rates and growth rates or as the "compactness" (that is, the formation of new nuclei around the old ones), can be the result of superimposition of several factors which alter the reactivity of the initial substance.

Depending upon the nature of the long-range action of various factors due to autolocalisation, in some instances there will be growth of the nuclei which are formed, and in others there will be a change in the compactness. Therefore in any investigation in the field of topography of solid-state chemical reactions and in particular of thermal decompositions, it is important to investigate the contribution being made by each factor to the change in reactivity around the growing nucleus. The directed regulation of the development of topochemical processes not only in time but also in space is a possibility. This would permit the regulation of the morphological properties of the solid product formed, which is important in the use of thermal decomposition in the preparation of catalysts for obtaining highly active oxide masses in the metallurgy of rare metals, in the preparation of ceramic materials of the ferrite type, etc. Finally, the development of these studies can even lead to the creation of technological processes new in principle, in which the stages of the production of a substance and the formation of articles from it will be combined.

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Institute of Chemical Kinetics
and Combustion, Siberian
Division of the Academy of
Sciences of the USSR,
Novosibirsk

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Mass Spectra of Organometallic Compounds of Group IVb

V.Yu.Orlov

Characteristic features of the dissociation of ions of organometallic compounds with silicon, germanium, tin, and lead are considered. Cyclic compounds are discussed separately; results on the following aspects are surveyed: rearrangements, metastable and multiply-charged ions, products of ionic-molecular reactions, and also the mass spectra of negative ions and correlations between ion decomposition processes and the thermal decomposition of the molecules of the compounds concerned.
There is a bibliography of 115 references.

INTRODUCTION

The development of the chemistry of the organometallic compounds of the Group IVb elements stimulated interest in their mass spectrometric investigation, occasioned by the uniqueness of their mass spectra, by the practical objectives of the structural analysis of these compounds, and also by the correlations observable between the breakdown of the ions in the chamber of the mass spectrometer and processes such as thermolysis. Hundreds of derivatives of silicon, germanium, tin, and lead have been studied in recent years; the mass spectra of over 300 compounds were published in 1968—1970 alone. The number of papers decreases appreciably with increase in both the atomic number of the metal and the number of metal atoms in the molecule; most of the investigations relate to compounds of the R_4E type, where R stands for alkyl, aryl, and other substituents, and also to the trimethylsilyl derivatives of all possible compounds.

Although the general rules of dissociative ionisation also extend to organometallic compounds, the presence in the molecule of one or more Si, Ge, Sn, or Pb atoms confers considerable singularity on the mass spectra. Review papers[1-3] have mentioned a series of features of the mass spectra associated with the decrease in ionisation potentials and bond strengths of the metal atoms on going from C to Pb, such as charge localisation on metal-containing species, intensive rearrangements, and abundance of metastable and multiply-charged ions.

The present review examines certain features of the mass spectra of the organometallic compounds of Group IVb with an account of recent results. A quarter of the papers cited in this review are from Soviet investigators.

GENERAL SCHEME OF DECOMPOSITION

Almost all the ionic current in the mass spectra of these compounds is carried by species which contain a metal atom (atoms). There is every basis for assuming that, in even-electron ions at least, the charge is localised on the metal atoms. This agrees with the fact that doubly and triply charged ions are usually observed solely for compounds which contain respectively not less than two or three metal atoms[4-6]. The fraction of hydrocarbon or other organic metal-free ions in the mass spectra of organometallic compounds with a single metal atom usually does not exceed a few per cent; it is even less for more complex molecules. This is connected with the low (in comparison with carbon) ionisation potentials of the atoms Si, Ge, Sn, Pb (respectively[7] 8.15, 7.88, 7.34, and 7.42 eV), the orbitals of which make a large contribution to the higher occupied molecular orbitals[3]. Only when the species formed are extremely stable metal-free fragments (usually aromatic) which are characterised by a low ionisation potential can the latter make a significant contribution to the total ionic current. Such are, for example, the fluorocarbon ions in the mass spectra of $(C_6F_5)_4Si$, $(C_6F_5)_4Ge$,[8,9] and the $[(C_6H_4)_2O]^+$ ion in the mass spectrum of SnSn-dichloro-oxastannadihydroanthracene[10]. Hydrocarbon ions observable in the mass spectra of organometallic compounds are characterised by considerable unsaturation (C_nH_{2n-3}, etc.).

The presence of many rather intense metastable ions in the mass spectra of organometallic compounds allows a genetic connection to be found between many fragment ions at the individual stages of the dissociation and is widely used for compiling decomposition schemes for the individual molecular ions. However, caution must be observed in doing this[3]. When a cascade (series) of metastable transitions $A^+ \rightarrow B^+$, $B^+ \rightarrow C^+$, $C^+ \rightarrow D^+$, is observed simultaneously then in addition to this there can also exist rather rapid direct transitions of the type $A^+ \rightarrow C^+$, $B^+ \rightarrow D^+$, $A^+ \rightarrow D^+$, not reflected by breakdowns of metastable ions; in addition, as estimates for some fragment ions of n-alkanes show, series of successive breakdowns composed of observable metastable ions, can lead to increased appearance potentials[11].

The intensity of the molecular ions for acyclic compounds of Si, Ge, Sn, or Pb is usually low[12-21], although higher than that of their hydrocarbon analogues[22]. It is significant only for certain heterocyclic compounds and for molecules with aromatic groups.

The first stage of the decomposition of the initial cation-radical is almost always the detachment of the radical; in the presence of several substituents the most weakly bound (usually, the heaviest[23,24]) group is detached first. One of the bonds with a metal atom is the weakest here. The even-electron ion that is formed is the origin of the remaining lighter fragment ions. For certain compounds (aromatic, heterocyclic) only is a significant part played by the primary splitting of molecules—C_6H_6 from Ph_3GeH, Ph_2 from Ph_4Ge, $[PhCH_2]_2$ from *m*- and *p*-Tol_4Ge, C_2H_4 from sila- and germa-cycloalkanes and spiranes with a central metal atom, etc.[25-33], however, usually these processes are characteristic solely for the subsequent stages of the decomposition. Further decomposition also usually leads to an even-electron ion, and the neutral fragments in its composition correspond to molecules of alkenes, alkanes, aldehydes, water, and other (including organometallic) compounds, some of which are unstable (considered in more detail below)†. The detachment of a

†The splitting of neutral hydrocarbon fragments from molecules with an alternative chain (for example, from cyclocarboxyloxanes[34]) proceeds primarily at the organic framework of the molecules and not the methyleen links.

radical from an even-electron ion, especially for organosilicon compounds, is seldom observed; in addition to the examples given by Chambers and coworkers[2] the following decompositions can be added:

$$[Me_3Si_3(CH_2)_3]^+ \rightarrow [Me_4Si_3]^{+\cdot} + C_2H_2^{\cdot}\ (Ref.28),$$

$$[(CH_3)_3SiCH_2CHCH_2]^+ \rightarrow [CH_2CHSiCH_2CHCH_2]^{+\cdot} + H^{\cdot}\ (Ref.20),$$

$$[Tol_{9,11}Ge_4]^+ \rightarrow [Tol_{8,10}Ge_4]^{+\cdot} + Tol^{\cdot}\ (Ref.35).$$

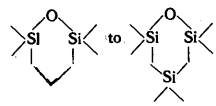
On going from compounds of silicon to compounds of tin or lead, the dissociation, and particularly the successive detachment of radicals, are less dependent upon the fragments formed having an even number of electrons[31,36]. The maximum intensity of the ions is shifted to the lighter ions of the mass spectrum; in particular, the intensity of the E^+ ions increases[2,31]. The number of decomposition paths decreases and the spectrum is simplified (it is made more "selective")[9,20,31,37].

CYCLIC COMPOUNDS

Let us examine in somewhat greater detail the cyclic compounds which occupy an important place in the chemistry of the transition elements of Group IVb; cyclic organosilicon compounds and heterocyclic compounds with metal atoms in the ring have been reviewed before[38,39].

The decomposition under electron bombardment of about a hundred cyclic compounds of Si, Ge, Sn, and Pb has been studied recently. They include cyclo-silanes, -germanes, and -stannanes of general formula $(R_2E)_n$ (R = Me, Ph, *p*-Tol; *n* from 5 to 7 [35,40-43]), cyclo-siloxanes and -germoxanes $(R_2EO)_n$ (R = Me, Pri; $n = 3-5$ [6,15,16]), cyclocarbosiloxanes $(R_2Si)_n(CH_2)_mO_{n-m}$ (where R = Me, $n = 3$ or 4, $m \leqslant n$ [34]), cyclocarbosilanes $(R_2SiCH_2)_n$ (R = H or Me, $n = 2-4$ [44,45]), cyclosilazanes $(R_2SiNR')_n$ (R = Me; R′ = H or Me_2ClSi; $n = 2$, 3, or 4 [46]), tetra-aza-3,6-disilacyclohexanes $[MeRSi(NR')_2]_2$ (R = Me or Vin; R′ = Ph, *m*-Tol, or *m*-Anisyl[47]), 1,4-disila- and 1,4-digerma-cyclohexadienes $[R_2E(CR')_2]_2$ (R = Me, Et, I; R′ = H, Ph [48]), sila- and germa-cycloalkanes $R_1R_2E(CH_2)_n$ ($R_1 = R_2 = H$; $n = 3$ or 4 [25,26]; R_1, R_2 = H, CH_3; $n = 3-5$ [27,28]; R_1, R_2 = H, C_3H_7, C_4H_9, C_6H_5, C_2H, Cl, Br [29,30]), germacyclopentenes[30], disila- and digerma-cyclopentanes $M_4E_2(CH_2)_3$,[28] sila-, stanna-, and plumba-spiroalkanes[31-33], derivatives of anthracene and phenanthrene[10,49-52], disilabicyclo-octadienes[53], tetrasila-adamantanes[54], cage polysilanes and carboxyloxanes[55,56], and certain other compounds[57-59].

Most of the cyclic organometallic (like organic) compounds show a marked resistance to dissociation, which appears in an increased intensity of either the molecular ion or of ions which contain the complete cyclic skeleton of the molecule. The molecular-ion peak is significant in the mass spectra of several compounds but it appears as the base (maximal) peak solely in the mass spectra of the cyclic organosilicon molecules with aromatic groups and 1,4-disilahexadienes[47,48,51,56,57,59]. On the other hand, in the mass spectra of cyclosiloxanes, cyclocarboxyloxanes, cyclosilazanes, and other molecules with an organic skeleton the intensity of the molecular ions is negligible, but the removal of one radical (or, respectively, of two radicals for doubly-charged ions) stabilises the $[M-R]^+$ residue, since it gives the base peak. This ion dissociates further very little and its decomposition is mainly connected with the elimination or organic molecules with retention of the initial organometallic skeleton of the molecule[6,15,16,34,44-46]. The intensity of the molecular ions also depends on the size of the initial molecule, falling markedly as the number of units is increased within the limits of a single homologous series, for example[45], for cyclocarbosilanes $[Me_2SiCH_2]_n$ from ~10% of the total ionic current at $n = 2$ to less than the error of measurement at $n = 3$ or 4. With a further increase in the number of units there is an increase in the intensity of the ions formed by breakdown of the $[M-R]^+$ ion[6,34]. The replacement of CH_2-groups by an oxygen atom in cyclocarboxyloxanes reduces the probability of decomposition associated with the destruction of the cyclic structure and the spectrum becomes more selective. The change from



leads to a marked decrease in the intensity of both molecular and also the fragment ions lighter than $[M-Me]^+$.[34,58]

For monosila-, disila-, and mono-germa-cycloalkanes[25-30,58] and for spiro-compounds with a central metal atom[31-33] the structure of which includes the $-[CH_2]_n-$ chain the decomposition is primarily due to the loss of molecules of C_2H_4, C_3H_6, or their combinations; its products are ion-radicals. On going from silicon to tin and lead in the spiro-compounds this process becomes the only decomposition process, and the fraction of even-electron ions in the mass spectrum falls to 4% for $[CH_2]_4 > Pb < [CH_2]_4$.[33]

REARRANGED IONS

There have been repeated reports[2] of the ease of occurrence of rearrangements which are accompanied by the dissociation of organometallic compounds, greatly impeding their mass-spectral structural analysis. There may be no corresponding rearrangements of the ions for carbon analogues[60]. In certain instances almost the entire mass spectrum is formed by rearranged ions (for example, decamethylcyclopentasiloxane[6]). The activation energies of reactions which lead to the formation of rearranged ions are evidently lower than those for reactions which can be purely dissociative[61]; many rearrangements of excited ions may occur without any activation energy.

There is no strict classification of ionic rearrangements but our compounds can be conveniently divided according to the observed effects into: (1) those leading to the migration of organic groups, and (2) those which are "skeletal". This division is provisional since the two types of process are often closely related (they may occur simultaneously), and in small molecules essentially the same, so that several rearrangements can be formally assigned to both "types" (for example, see Kuivila and coworkers[62]); however, such a classification is frequently sufficiently unambiguous. The rearrangements or migrations of organic groups is extremely widespread in the mass spectra of organometallic compounds; they play the same part in these compounds as hydrogen rearrangements in the mass spectrometry of organic compounds and accordingly, on the same basis can be regarded as distinct from "skeletal" rearrangements. It is noteworthy that hydrogen rearrangements are frequently indissolubly linked with "skeletal" ones[63].

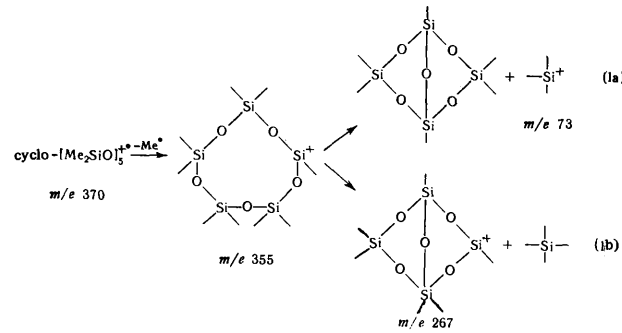
Migration of Groups

It would be difficult to list all the many examples of the migration of organic groups in the ions of Si, Ge, Sn, and Pb derivatives. From the results of recent years we will mention only certain observations of the migration of methyl[59], methoxy-[64], phenyl[65], and other organic[16,19] groups. We emphasise that the frequently observed ion of type R_3E^+ (E = Si, Ge, Sn, or Pb) which gives an intense, and in many instances the base peak, is rearranged to a considerable extent or completely, although frequently it could formally be formed also by simple breaking of a single bond (removal of a terminal group). The rearranged ions R_3E^+ are intense for cyclic compounds of the type $[R_2E]_n$ (where R = Me, Ph, Tol; E = Si, Ge, Sn [35,40,41,43]), $[R_2EO]_n$ (R = Me, E = Si [6] and at $n = 5$ the Me_3Si^+ ion gives a base peak and R = Pr^i, E = Ge; in the last instance the investigators[15] assigned the intense peak of the $Pr^i_3Ge^+$ ion to impurities!). Among ions of the R_3E^+ type are compounds $^1R^1_3E.^2E^2R_3$, where ^1R and ^2R are alkyl or aryl, and ^1E or ^2E are Si, Ge, or Sn, which contain all possible combinations of R and E.[66-69]. Investigation of rearranged ions in methylsiloxanes with trideuteromethyl terminal groups[70] showed complete rearrangement of the methyl groups at all the ions so that the mass spectrum in this instance is insensitive to the sites of the isotopic label (CD_3). This phenomenon is observed irrespective of the conditions of ionisation both in the decrease in the energy of the electrons up to a threshold, and in the ionisation of the molecules in collisions with metastable excited argon atoms. What has been said relates to all the most intense ions of the siloxanes, the formation of which does not require the breaking of C—H bonds; here the CD_3 groups migrate as a whole. However, for ions the formation of which requires the breaking of C—H bonds (the peaks of these ions are weaker in these mass spectra), a complete set of all possible combinations of H and D is observed, that is, hydrogen rearrangement also takes place‡. In this manner the breaking of one bond or another is indistinguishable from the corresponding rearrangements.

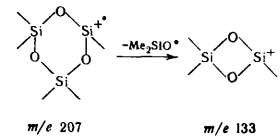
The migration of larger groups such as trimethylsilyl (TMS) has been observed for more complex molecules; here, however, the possibility of skeletal rearrangements, in particular, cyclisation, is usually considered simultaneously[72-76].

Skeletal Rearrangements

Such skeletal rearrangements as the contraction or enlargement of rings or the formation of a new ring are well known in the mass spectrometry of organic compounds, especially heteroatomic compounds[63,77]. The role of these processes in the mass spectrometry of organometallic compounds, especially rather complex ones, increases appreciably. The possibility of the enlargement of a four-membered to a five-membered ring was advanced as an explanation of the similarity in the mass spectra of dimethylsilacyclobutane and methylsilacyclopentane[27]; ideas about the contraction of the ring were used for the interpretation of intense fragment ions in the mass spectra of cyclic siloxanes, carbosiloxanes and tetra-azadisilacyclohexanes[6,34,47]. For cyclosiloxanes, in particular, the formation of bicyclic structures for both positively charged and neutral fragments is possible; the decomposition scheme of, for example, decamethylcyclopentasiloxane, can be represented as follows:



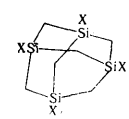
The cyclic structure of the ion $(SiO)_2$ (m/e 133) in the decomposition



is confirmed indirectly by its possessing (judging from the width of the corresponding metastable peak) an appreciable kinetic energy (~1 eV), which shows the considerable stability of the fragments formed.

Cyclisation of acyclic structures is often advanced as an explanation of observed rearrangements[71-73], etc. Especially convincing results which support the existence of this phenomenon can be found in the mass spectra of linear siloxane and carbosilane chains[6,45]. Almost all the fragment ions of sufficiently long siloxanes are formed in the cyclisation of either charged or neutral fragments. The mass spectra of the linear siloxanes contain all the elements of the mass-spectra of the corresponding cyclic molecules, including all the fragment and metastable ions and they could easily be taken for impurity ions if the corresponding multiply-charged ions were not absent. This phenomenon is analogous to the cyclisation of linear polysiloxanes on heating. The formation of an m/e 207 peak in the mass spectra of R_3AsO_3, R_3AsO_4, and R_3PO_3, where R = TMS (this is the base peak for R_3AsO_3) is undoubtedly connected with the cyclisation of ions[75].

There is evidently a connection between the skeletal rearrangement of tetrasila-adamantanes



where X = H, D, or Cl and of the cage polysilanes $Me_{2n-2}Si_n$ (n = 8, 9, or 10), and the appearance in their mass spectra of intense peaks of $[M-CH_3]^+$ (hydrogen rearrangement)[54] and $[M-Me_3Si]^+$ [55] ions; $[M-Me_3Ge]^+$ ions are typical for permethylcyclopolygermanes[48].

Geometrical factors are essential in the formation of new bonds[78]. In sufficiently rigid molecules rearranged ions are formed only when the interacting groups are

‡ A similar conclusion follows from the results obtained in the investigation of rearrangements in tetraphenylsilanes labelled with deuterium[71].

favourably situated. The migration of TMS groups, which gives intense peaks or rearranged ions in the mass spectra of TMS-derivatives of steroid phosphates does not occur when there is a considerable spatial separation of the corresponding groups; in this instance a hydrogen rearrangement prevails[79]. The mass spectra of TMS diethers of the type $Me_3SiO[CH_2]_nOSiMe_3$ (n = 10, 22) are characterised by the presence of the rearranged $Me_3SiOCH_2O_3SiMe_2$ ion, formed by the elimination of the central part of the molecule—almost all of the hydrocarbon chain, but, as the spectra of molecules labelled at one end with CD_3 groups show, there is no exchange of methyls between the TMS groups[80].

The examples of reactions (1a) and (1b) clearly show the connection between the skeletal rearrangements and the migration of the organic groups. Essentially, there is a single process of bond rearrangements (in this instance two bonds are broken, Si—O and Si—C and two such bonds are formed anew). Evidently, the rapid single-stage electronic process of bond migration in an electronically excited ion plays at least a significant part if not the determining one; after it follows the migration of the newly connected parts of the molecular ion.

However, it is possible that the comparatively high intensity of the rearranged ions in the mass spectra of organometallic compounds could be linked with the general retardation of the decomposition (see below); both are characteristic of the same compounds. Then the vibrational excitation of the ion facilitates the rearrangements which are dependent upon the necessary approach of the interacting parts of the molecular ion.

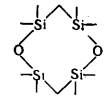
PRODUCTS OF IONIC MOLECULAR REACTIONS

In the mass spectrometric investigation of either individual organometallic compounds or of their mixtures with other substances it is necessary to take into account the possibility of distortion of the mass spectra by the products of ion-molecule reactions. The reactions of intense fragments of metal-containing ions with the molecules of a gas proper or of other compounds, leading to the intermolecular transfer of complex groups, are characterised by large effective profiles and proceed with appreciable yields at elevated or ordinary pressures in the ion source of the mass spectrometer.

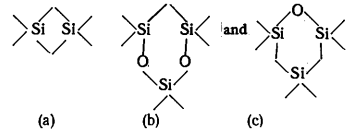
Heavy ions of the type $[M + 73]^+$, $[M + 147]^+$, etc. up to the very weak $[2M - 15]^+$ are recorded in the mass spectra of individual compounds, such as the TMS derivatives of glycerophosphates and other biologically active substances[81,82]. In the mass spectra of mixtures of compounds of the R_4E type (R = Me, Pr, or Bu; E = Si, Ge, or Sn) and Me_3SiR_1 (R_1 = OTMS, NHTMS, OMe) with a whole series of organic compounds which contain an electron-withdrawing group, ions of the $[M + A]^+$ type, where M is an organic molecule and A corresponds to R_3E^+, H_3E^+ and other intense fragment ions of these organometallic compounds, were observed[83]. The ratios of the intensities of the heavy ions for comparatively light A roughly follow the relations for fragment reagent ions; the intensity of $[M + A]^+$ falls with increase in the complexity of A.[82] (The peaks of the molecular ions R_4E^+ and $Me_3SiR_1^+$ are extremely weak.) The masses of the heavy ions (including the labelled ones) show that the heavy ions are formed by the simple addition of fragment ions A^+ to neutral molecules. Published results[83] reveal that the profiles of such reactions for even-electron fragment ions are much larger than those for the ion radicals.

DISSOCIATIVE IONISATION AND THERMOLYSIS: MASS-SPECTRAL RESULTS ON UNSTABLE AND "NONEXISTENT" COMPOUNDS

An analogy between dissociative ionisation and the thermal decomposition of molecules has been noted repeatedly (it is naturally assumed that the last process proceeds under conditions of unimolecularity). Although these two processes differ in principle, due to the nature and magnitude of the excitation energy, with the properties of the charged species, the conditions of observation, etc., their comparison shows a series of common features connected with the combination of electron-vibrational processes of bond migrations in ions and molecules, above all the similarity of the sets of reaction products and also the correlation between the temperature dependence of the thermolysis and the appearance potentials of the corresponding ions[84]. A series of correlations of thermolysis and "electronolysis" was also noted for organometallic compounds. Thus on the one hand the thermal rearrangement of cyclocarboxyloxane (I)


(I)

leads to the formation of smaller rings[85]:



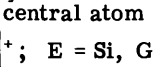
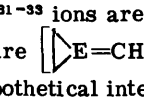
and on the other in the mass spectrum (I) there are ions which correspond to the ions of the $[M - CH_3]^+$ type of molecules (a)—(c). The similarity in the thermolysis and dissociation of a molecular ion in electron bombardment was noted for dimethylsila- and mono-germa-cyclobutanes[86]; in both processes the initial species lose C_2H_4 and C_3H_6, and the relative probability of decomposition with loss of C_3H_6 is considerably greater for germacyclobutane both in electron bombardment and in thermolysis. A similarity in the ratios of the probabilities of removal of C_2H_4 and C_3H_6 in thermolysis and electron bombardment is also observed for the disila- and digerma-cyclopentanes[28].

Comparison of thermolysis and dissociative ionisation is especially interesting in instances when the mass spectra allow the existence of unstable species postulated as intermediate reaction products to be guessed or confirmed to a certain extent. Among such substances there is considerable interest in the compounds of the bivalent elements of Group IVb§, including derivatives of silicon(II).[87] Compounds with multiple bonds are another type of unstable derivatives of these elements. The interest in these derivatives is due, on the one hand, to the fact that there is yet no satisfactory theoretical explanation of the inability of the Group IVb elements to form stable multiple bonds similar to the bonds in alkenes and carbonyls[89] (the calculations show the possibility of synthesis and separation of compounds with a double bond, in

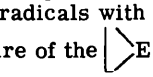
§ The oxides SiO, GeO, SnO, and PbO and their oligomers were separated by matrix isolation[88].

particular, Si=Si.[90] On the other hand, the assumption of the existence of intermediate compounds with a double $(p-p)\pi$-bond allows the mechanism of such reactions as the thermocondensation of monosilacyclobutanes[91,92], thermal changes in the gas phase of cyclocarboxyloxanes and cyclosiloxanes[93-95] to be explained easily; in this species such as $Me_2Si{=}CH_2$ and $Me_2Si{=}O$ are postulated. Indirect experimental confirmation of the existence of the unstable product $Me_2Si{=}CH_2$ was obtained recently[96]. The thermal removal of ethylene by germacyclobutane evidently proceeds just as for silacyclobutane and the thermocondensation to digermacyclopentane probably includes the formation of carbenoid species of the Me_2Ge: type[86]. In connection with this it is desirable to consider the mass spectral results about species of this type. Under the conditions of observation in the mass spectrometer they can be either ion-radicals or even-electron neutral molecular groupings.

The first report of the observation in the mass spectra of siloxanes of species of the dialkylsilanone type, made more than 20 years ago by Andrianov and Sokolov[97], must be regarded above all as the prediction of the existence of such species, since the investigators, using the comparatively imperfect mass spectral technique of that time, evidently took for the hypothetical silanones the even-electron fragment ions (mainly rearranged ones) usual for these compounds[6].

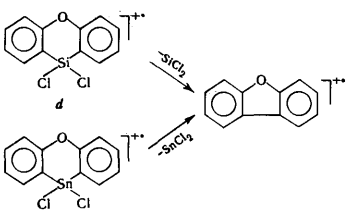
When the ionised species have sufficient energy the mass spectrum includes ions so deeply dissociated including ion-radicals formally corresponding to the bivalent metal. The appearance potentials of such ions are usually higher than those of the neighbouring odd-electron ones. Therefore it is interesting here to consider only those instances when the intensity of such ions is sufficiently high. As an example there is the ion $[R_2Si{:}]^+$ in the mass-spectra of the phenoxasilins[50], $[C_2H_4E]^+$ in the mass spectra of spiro-compounds with a metal central atom (the possible structure is  ; E = Si, Ge, Sn, Pb [29,31-33]). Among the ions for which the presence of an E=X double bond (X = C or O) can be postulated are ions of the type $[R_2E{=}CH_2]^+$, which give extremely intense (or maximal) peaks in the mass spectra of the dialkylsila- and dialkylgerma-cyclobutanes[27-29]. In the mass spectra of the spiro-compounds[31-33] ions are released which can be assigned the structure  , which agree with the structure of the hypothetical intermediate product of the thermolysis of silaspiroheptane[98].

Ion radicals of the silanone type were not observed in the mass spectra of siloxanes.

Ion radicals with a composition which corresponds to a structure of the  type (significant but not exceeding in intensity the neighbouring even-electron ions) were observed in the mass spectra of 1,2-disila- and 1,2-digerma-cyclopentanes[28]. However, in other instances the peak of the $[Me_4Si_2]^+$ ion is maximal[53]. Ions of this type are also intense in the mass spectra of 1,4-digermahexadienes[48,99].

The mass spectral results on the formation of neutral fragments of this type may be of great interest for comparison with chemical results. Since the information about neutral fragments is confirmed or is obtained on the basis of an examination of the decomposition of metastable ions, which proceeds in times of the order of more than 1 μs, it can be presumed that neutral species live for at least as long. This corresponds closely to the non-excited state. The composition of the neutral metal-containing fragments, found as the difference in the composition of the initial metastable ions and fragment ions, obtained as a result of a single-step change, usually corresponds to the composition of the molecules—both those known and often those unknown in the free form.

Bivalent metals correspond to neutral fragments of the R_2E type—Me_2Si, MePhSi, eliminated in the decomposition of the disilanes[69], Me_2Ge in the decomposition of methylpolygermanes[19,43] $(p\text{-Tol})_2E$ (where E = Si or Ge) in the decomposition of tolylcyclo-silanes and -germanes[35], $SiCl_2$ and $SnCl_2$ in the decompositions[10,51]:



10,10-Dimethyl- and 10,10-diphenyl-phenoxysilin eliminate the lower oxide of silicon, SiO.[50] The same group is lost in the last stages of the decomposition of the cyclosiloxanes and also certain linear siloxanes after the loss of a large part of the organic framework[6].

The species, the composition of which corresponds to the formula R_2EX (X = CH_2, O, etc.) can be assigned structures such as REXR, which corresponds to a bivalent metal, or structures with the $R_2E{=}X$ double bond. The latter may be stable. They correspond in particular to the hypothetical dialkylsilanones. Information is available on the formation of the neutral fragments H_2SiO,[50,51] Me_2SiCH_2,[34] Me_2SiO,[6] Cl_2SiO,[51] Me_2GeO [15,16] (including instances when this species is not a unit of the molecule investigated—cyclo-$[Pr^i_2\,GeO]_3$ [15]). In siloxanes neutral fragments of the Me_2SiO type are eliminated, evidently solely when the formation of the usual oligomers $[Me_2SiO]_{3,4}$ is impossible.

INTENSITY OF METASTABLE IONS AND GENERAL RETARDATION OF THE DECOMPOSITION OF THE IONS OF ORGANOMETALLIC COMPOUNDS

Interest in metastable ions is usually restricted to the information which they can give about paths and distinct steps in the decomposition, allowing a scheme of successive decompositions to be drawn up (in general, however, insufficiently well founded, as shown above). Here the intensity of the metastable ions is usually not measured and its magnitude is not taken into account at all. Furthermore the relative intensity of the metastable ions in the mass spectra of the organometallic compounds is usually quite significant in even an approximate calculation of the breadth of the corresponding peaks¶. Thus the ratio I_m/I_0 of the sizes of the "metastable" peak and the "ordinary" peak of the decomposition product reaches ~0.1 for the reaction

$$Me_{13}Si_6O_5^+ \rightarrow Me_7Si_3O_2^+ + (Me_2SiO)_3$$

¶ Precise calculation is difficult because of the differing effectiveness of the collection of ions which decompose in the ion source and in the analyser.

in tetradecamethylhexasiloxane and 0.2 for reaction (1b) in decamethylcyclopentasiloxane[6]. Hence these are significantly retarded on the average.

The lifetime of metastable ions of derivatives of the Group IVb elements was not measured specially; it was noted that in a mass spectrometer with double focussing the number of recorded metastable ions which decompose between the ion source and the first (electrostatic analyser, is several times greater than the number of ions which decompose between the first and second (magnetic) analysers. The number of metastable ions of the last type falls from Si to Ge and Sn (6—3—1).[20] Evidently, the total retardation of the decompositions which are characterised by the total relative intensity of the metastable ions increases from C to Si and then falls again from Si to Sn and Pb.

The ratio I_m/I_0, which characterises the relative probability of the metastable breakdown, can vary strongly for different paths of dissociation; for siloxanes the lower value of the ratio corresponds to a path leading to the formation of a lighter ion. For example, for reaction (1b) (formation of the ion m/e 267) $I_m/I_0 = 0.2$ and for (1a) (ion with m/e 73) $I_m/I_0 = 0.02$.

MULTIPLY-CHARGED IONS

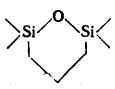
As noted in a recent study[100], the factors which determine the intensity of the doubly-charged ions and the path for their decomposition are "extremely complex and do not support widely used generalisations". In this connection a brief review of the empirical results on multiply-charged ions in the mass spectra of the organometallic compounds should be of interest.

The presence of multiply-charged ions in the mass spectrum of a complex molecule can be regarded as the appearance of its resistance towards dissociation or the retardation of the latter. The role of stabilising features in organic molecules usually brings about stable aromatic structures—this is so in particular for all the organic compounds for which triply-charged ions are observed. However, doubly- and triply-charged ions are characterised for the mass-spectra of organometallic compounds which contain respectively not less than two or three metal atoms in the molecule†. Intense peaks of multicharged ions are recorded in the mass spectra of methylsiloxanes[4,101,102] paraffins substituted with two TMS groups[5], silazanes[46], and other compounds which contain more than one metal atom[58,59,103]. Evidently the charges of multicharged ions are localised on different metal atoms.

For the heaviest of the observed multicharged ions usually $m/e = \frac{M}{n} - R$, which corresponds to the loss from the molecule M of a number of radicals R equal to the ionisation multiplicity n. Evidently these radicals are removed from the metal atoms on which the charge is localised, as is shown by the loss of valence electrons by these atoms. The stability of the multicharged ions is much greater when the metal atoms are separated by atoms or groups: O, CH_2, NH, etc.[104] and the effect of the oxygen atoms on the stabilisation of the multicharged ions is stronger than that of CH_2 groups. Thus the intensity[28,58] of the doubly-charged ions of the type $[M - 30]^{2+}$ is 1% in

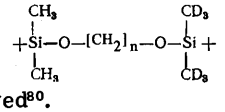


and 4% in



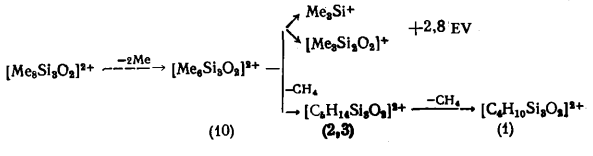
for cyclocarboxyloxanes it increases twofold when all the CH_2 groups are replaced by oxygen atoms in the Si_3 molecules and threefold in Si_4 molecules[34]. Oxygen has the same effect in germanium compounds: the intensity of the doubly-charged ions from digermoxanes is higher than for the analogous digermanes[16]. The role of connecting groups in the stabilisation of multicharged ions can be determined by factors such as the increase in the distance between the charges and their delocalisation at the electronic orbitals of the connecting atom, strengthening the effect of $p_\pi - d_\pi$ conjugation for N or O. In individual instances, for the especially stable six-membered cyclic molecules it is possible to observe doubly-charged ions of the $[M-R]^{2+}$, obtainable in the breaking away of only one radical (considerably less intense, however, than ions of the $[M - 2R]^{2+}$ type)[34,58,103]. The intensity of the $[M - 30]^{2+}$ ions of the bistrimethylsilyl derivatives of the amino-oxynaphthalenes depends on the position of the substituent[105].

Multiple ionisation with localisation of charges on various metal atoms is evidently linked with the migration of charges (excitation) to these atoms. Charge migration in a hydrocarbon chain proceeds with minimal barriers[106] and is controlled by the ionisation potentials of the various parts of the molecules[107,108]. For chains with two Me_3SiO groups at the ends, one of which is completely deuteriated, the doubly-charged ions formed in the loss of two methyl groups from different silicon atoms



are readily observed[80].

Multiply-charged ions decompose according to two paths—with and without sharing of charges. The peaks of corresponding metastable ions are often observed; their form shows the nature of the process—in decomposition with charge sharing, which is accompanied by the release of a considerable kinetic energy, broad peaks with flat tops are obtained. The width of the peak allows the energy of the decomposition process to be estimated[109,110]; on taking into account that it is determined by the coulombic repulsion of the charges, the position of the latter in a multicharged ion and its configuration can be found. For example, doubly-charged octamethyltrisiloxane ions decompose according to the scheme:



(the numbers in parentheses give the relative intensity in percentages of the main singly-charged ion $[M - 15]^+$; the continuous arrows show the changes confirmable by metastable ions). The total energy of 2.8 eV of the singly-charged fragments of a doubly-charged ion corresponds to a charge separation of ~5 Å, which is close to the distance between the extreme silicon atoms in this molecule (5—6 Å, depending upon the conformation)[102].

The other path for the decomposition of multiply-charged ions (including triply-charged ones) is the splitting, usual for singly-charged ions, of neutral fragments,

† Doubly-charged ions GeH_2^{2+}, GeH^{2+}, and Ge^{2+} have been recorded for GeH_4.[16]

including those associated with rearrangements. Thus for the doubly- and triply-charged ions of the linear methylsiloxanes a series of fragment ions obtained by successive removal of two or three methane molecules formed from the organic framework of the molecule[94,102]. Since such a process is energetically less favourable than decomposition with charge division it shows the considerable stability of the siloxane skeleton of the multiply-charged ions. The slow decompositions of this type, which are observed, for example, for the Si_2 and Si_3 linear siloxanes[102], are especially remarkable[102]. In organic mass spectrometry similar results are known only for stable aromatic compounds[111].

NEGATIVE IONS

There have been only a few mass spectrographic studies of the negative ions of the organometallic compounds of Group IVb. An intense molecular anion-radical with a resonance maximum at electron energies not exceeding a few eV was observed for dodecamethylcyclohexasilane; for Me_6Si_2 the molecular anion was two orders of magnitude weaker and for Me_6Si_2O it was not observed at all[112]‡. A molecular anion was also not recorded in the negative mass-spectra of the tetramethyl derivatives Me_4E (E = Si, Ge, or Sn); however, for E = Si or Sn the intense ions $[M - 1]^-$ with resonance maxima at 4 and 7.8 eV and at 8 eV respectively, stabilised with $p_\pi - d_\pi$ interaction with the vacant orbitals of the central metal atom[114]. For E = Ge or Sn, Me_3E^- ions are characteristic; lighter fragment ions were also observed[114,115]. The main process for the decomposition of the negative ions of the tetraphenyl derivatives (E = Si, Ge, Sn, Pb) is the loss of phenyl or diphenyl; hydrogen rearrangement also plays some part in the subsequent decomposition[71].

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‡ A stable anion-radical of the compound $(Me_2Si)_6$ was also obtained in the condensed phase[113].

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Phosphorylated Aldehydes†

A.I.Razumov, B.G.Liorber, V.V.Moskva, and M.P.Sokolov

The review presents systematic data on the methods of synthesis and chemical properties of phosphorylated aldehydes. Attention has been concentrated on organophosphorus compounds containing the formyl group in the alkyl substituent linked to the phosphorus atom by a C-P bond. The phenomena of keto-enol tautomerism of phosphorylated aldehydes are described in greater detail, the influence of various factors on the position of the keto-enol equilibrium is assessed, and the geometrical structure of the enols formed is considered.
The bibliography includes 120 references.

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I. INTRODUCTION

Aldehydes occupy one of the central positions in organic chemistry both as regards their reactivities and synthetic possibilities. Presumably phosphorylated aldehydes will in time occupy just as important a place in the chemistry of organophosphorus compounds. In view of the high reactivity of the aldehyde group, they may be considered as the starting materials for the synthesis of a wide variety of other organophosphorus compounds. On the other hand, compounds of this class are convenient for the investigation of many general theoretical problems in organic chemistry and the chemistry of organophosphorus compounds.

Although from the time of the publication of the first study [1] which laid the foundations of the research on phosphorylated aldehydes twenty years have elapsed, the accumulation of factual data in this field has been extremely slow. This is probably due to the lack of convenient methods of synthesis for compounds of this kind. However, in recent years the number of published investigations of this problem increased sharply. Together with the development of synthetic methods, studies have been made on the structures and reactivities of phosphorylated aldehydes.

Hitherto there have been no reviews in the literature dealing with phosphorylated aldehydes. This paper is a first attempt at a general and systematic account of the available data on this question. At the same time, we feel it would be useful to draw the attention of investigators to this interesting branch of organophosphorus chemistry.

The review is devoted to derivatives containing the formyl group in the alkyl substituent linked to phosphorus via C-P bonds but other formyl-containing organophosphorus compounds are also briefly considered.

II. METHODS OF SYNTHESIS OF PHOSPHORYLATED ALDEHYDES

The vast majority of methods for the preparation of compounds with a C-P bond are based on the interaction of phosphorus(III) acid esters with electrophilic agents. However, the high reactivity of the aldehyde group in relation to such esters hinders the direct introduction of the formyl-containing substituent at the phosphorus atom. Organometallic synthesis, frequently used to form C-P bonds, also cannot be used. Therefore the formyl group must be introduced or regenerated from derivatives after the formation of the C-P bond.

In 1952, Dawson and Burger [1] suggested for the first time that the fundamental method for the synthesis of organophosphorus compounds—the Arbuzov reaction—be used to synthesise phosphorylated aldehydes with a halogenoacetal as the electrophilic agent. The reaction of the diethylacetal of bromoacetaldehyde with triethyl phosphate yielded the diethylacetal of diethylphosphonoacetaldehyde, the acid hydrolysis of which led to diethoxyphosphonoacetaldehyde:

$$(EtO)_3P + BrCH_2CH(OEt)_2 \rightarrow (EtO)_2P(O)CH_2CH(OEt)_2 + EtBr$$

$$(EtO)_2P(O)CH_2CH(OEt)_2 \xrightarrow{H_2O(H^+)} (EtO)_2P(O)CH_2C(O)H + 2EtOH .$$

The authors failed to develop further this method (neither the phosphorylated acetal nor the aldehyde were isolated in a pure form; the latter was only identified in the form of its 2,4-dinitrophenylhydrazone), but their idea concerning the protection of the aldehyde group undoubtedly merited attention.

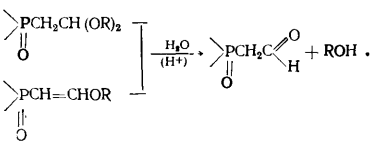
Detailed studies were made in our laboratory [2-8] of the reactions of halogenoacetals with phosphorus(III) acid esters followed by hydrolysis of the phosphorylated acetals to aldehydes up to the development of preparative procedures. Various phosphorus(III) acid esters (phosphites, aliphatic and aromatic phosphonites and phosphinites) together with a wide range of halogenoacetals were employed in the reactions. It was found that the influence of various factors [the nature of the phosphorus(III) acid ester and of the halogen in the halogenoacetals as well as the structure of the halogenoacetal] is determined by familiar relations typical for the Arbuzov reaction [9]. The temperature conditions in the reaction play a very significant role. At elevated temperatures phosphorylated aldehydes are degraded to the corresponding phosphorylated vinyl ethers:

$$>PCH_2CH(OR)_2 \xrightarrow[-ROH]{t^\circ} >PCH{=}CHOR$$

† Phosphonylated aldehydes (Editor of Translation).

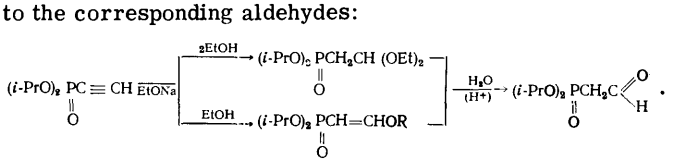
This type of degradation has also been noted in studies by other workers [10-12]. Probably the tendency of phosphorylated acetals to undergo reactions of this type is influenced, apart from the temperature factor, by the nature of the substituents at the phosphorus atom and the composition of the second component in the reaction mixture. Thus the reaction of tri-isopropyl phosphite with a chloroacetal (170°C) leads to the formation of a mixture of the phosphorylated acetal and alkoxyvinylphosphonate [10], while the interaction of a bromoacetal with trimethyl phosphite [11] and ethyl diphenylphosphinite [12] leads to the exclusive formation of the corresponding phosphorylated enolic ethers. It has been noted [11] that mainly ethoxyvinylphosphonate was formed in the study by Dawson and Burger [1].

The fact that phosphorylated acetals as a rule contain a mixture of the corresponding phosphorylated vinyl ethers is hardly a serious obstacle to the synthesis of phosphorylated aldehydes from them, since the hydrolysis of both the aldehydes and the vinyl ethers [10] leads to the formation of the same aldehydes:



In the hydrolysis of the phosphorylated acetal, a high concentration and a large excess of the acid should not be employed (to avoid the hydrolysis of the ester groups at the phosphorus atom). It is quite sufficient to use 5–7% HCl (80–90°C, hydroquinone). Naturally, as the electron-accepting phosphorus-containing group is removed further from the acetal group, the ease of hydrolysis increases. The excess acid and the volatile hydrolysis products should be removed *in vacuo* at relatively low temperatures. In the milder hydrolysis of phosphorylated acetals in the presence of ion exchangers, the yield of aldehydes increases [13].

The Michaelis–Bekker reaction can also be used to synthesise phosphorylated acetals [14]. Moreover, ethynylphosphonates react with alcohols in the presence of alkoxides with formation of a mixture of phosphorylated enolic ethers and acetals [10], the hydrolysis of which leads to the corresponding aldehydes:



The applicability of the method is limited by the availability of the ethynylphosphonate.

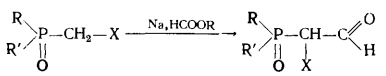
On the whole, one may say that the method of synthesising phosphorylated aldehydes via the corresponding acetals is general and has the advantage over the methods described below that it can be used to obtain products with various relative positions of the phosphorus atoms and the aldehyde groups as a function of the structure of the initial halogenoacetals and phosphorus(III) acid esters.

The genetic relation between vinylphosphonates and the corresponding phosphorylated acetals and the possibility of synthesising phosphorylated aldehydes on their basis was already noted above. The synthesis of vinylphosphonates was developed on the basis of the phosphorylation with phosphorus pentachloride of enolic [15] and dialkyl [16] ethers and acetals [17,18] as well as a number of other methods. It is clear that this method of synthesising phosphorylated aldehydes is based on the use of a fairly readily available class of compounds. The synthesis of phosphorylated aldehydes from the corresponding vinylphosphonates has also been thoroughly developed. Phosphorylated aldehydes belonging to the class of phosphonates [19-21], phosphonothionates [22,23], and phosphonothiolates [23,24] have been obtained by this procedure.

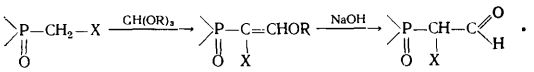
The hydrolysis of the corresponding alkoxyvinylphosphonates proceeds similarly to that of phosphorylated acetals but requires more severe conditions (particularly for phosphorothioic acid derivatives). This must be taken into account in the hydrolysis of acetals containing an admixture of a phosphorylated enolic ether. In practice the method is applicable only to the synthesis of α-phosphorylated aldehydes of the phosphonate series (in view of the availability of the initial enolic ethers).

In the synthesis of aldehydes with different relative positions of the formyl group and the phosphorus-containing substituent and also aldehydes belonging to the series of phosphinates and phosphine oxides, other procedures must be resorted to.

Many phosphorylated aldehydes have been obtained by the formylation of organophosphorus compounds with an active methylene group. The aldehydes synthesised include, together with the phosphorus-containing groups, other electron-accepting substituents in the α-position. Here one employs either direct formylation of the methylene group via the mechanism

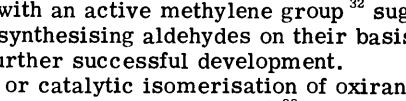


or the alkoxymethylene fragment is introduced by the initial interaction of the organophosphorus compound with orthoformic ester, this being followed by the alkaline hydrolysis of the condensation product:



The active methylene group in phosphonoethylacetate [1,25,26], phosphonoacetone [25], benzylphosphonate [27], cyanomethylphosphonate [28], chloro- and bromo-methylphosphonates [29], diphenylbenzylphosphine oxide [12], and dibutylethoxycarbonylmethylphosphine oxide [30] was formylated by the first procedure. The formylation of dibenzylphosphinous acid proceeds at only one methylene group [31]. The synthesis of phosphorylated aldehydes with the preliminary introduction of the alkoxymethylene group has been achieved from cyanomethylphosphonate [26], phosphonoacetone [29], and dibutylphosphinylacetone [30]. The above reactions yielded phosphorylated aldehydes containing phenyl, chloro-, bromo-, cyano-, alkoxycarbonyl, and acyl groups next to the formyl group. Aldehydes of the above series proved suitable for the investigation of keto-enol tautomerism, which will be described below. The wide variety and large number of organophosphorus compounds with an active methylene group [32] suggest that methods of synthesising aldehydes on their basis will undergo a further successful development.

Thermal or catalytic isomerisation of oxiranylphosphonates ("epoxyvinylphosphonates") [33] leads to phosphorylated aldehydes in fairly high yields:



Both aliphatic [34] and cyclic [34,35] phosphorylated aldehydes can be obtained in this way. Oxiranylphosphonates without substituents in the oxiranyl group show little tendency to isomerisation of this kind [35]. Thus diethyl oxiranylphosphonate cannot be isomerised to phosphonoacetaldehyde either by heating or by treating with boron trifluoride-ether. However, phosphonoacetaldehyde is formed in a yield of up to 10% during the epoxidation of vinylphosphonate in methanol with hydrogen peroxide. It remains obscure whether this is a result of a rearrangement of the epoxide or of some other reaction between vinylphosphonate and hydrogen peroxide. Another method for the preparation of oxiranylphosphonate is dehydrochlorination of β-chloro-α-hydroxyethylphosphonate; here small amounts of phosphonoacetaldehyde are also formed together with the main reaction product—oxiranylphosphonate [36]:

$$(EtO)_2P(O)CH(OH)CH_2Cl \xrightarrow[\text{(in alcohol)}]{KOH} (EtO)_2P(O)CH\text{-}CH_2 + (EtO)_2P(O)CH_2C(O)H .$$

Dehydrobromination of β-bromo-α-hydroxypropylphosphonic acid with sodium bicarbonate yields α-phosphonopropionaldehyde as the main reaction product [37]:

$$CH_3CH(Br)CH(OH)P(O)(OH)_2 \xrightarrow{NaHCO_3} (HO)_2P(O)CH(CH_3)C(O)H .$$

Thus oxiranylphosphonates or phosphorylated halogenohydrins can also be used to synthesise substituted phosphorylated aldehydes.

Apart from the methods of synthesis of phosphorylated aldehydes dealt with above, methods which have not hitherto found much application have been described in the literature. Of the studies of this series, the synthesis of aldehydes from compounds of the oxaphosphorane type [38,39] obtained as the result of the interaction of trialkyl phosphites with $\alpha\beta$-unsaturated carbonyl compounds should be mentioned:

$$(RO)_3P + CH_2{=}CH{-}C(O)H \rightarrow \text{oxaphosphorane} \xrightarrow{HOH} (RO)_2P(O)CH_2CH_2C(O)H .$$

Treatment of the phosphorane with acetic acid also yields phosphonopropionaldehyde. The interaction of phosphoranes with alcohols leads to the acetals of the corresponding β-phosphonopropionaldehyde [40]. When crotonaldehyde reacts with triethyl phosphite in the presence of ethanol, the corresponding acetal is formed mixed with the enolic ether [41,42]. Phosphonoacetaldehydes have been obtained by the hydrolysis of β-acyloxy-β-chloroethylphosphonates [43-45]. The required starting materials were obtained by the low-temperature reaction of vinyl acetate with phosphorus pentachloride:

$$CH_3COOCH{=}CH_2 + 2PCl_5 \rightarrow CH_3COOCHClCH_2PCl_4 \cdot PCl_5 \xrightarrow{SO_2} \rightarrow CH_3COOCHClCH_2P(O)Cl_2 \xrightarrow[\text{pyridine}]{2ROH} CH_3COOCHClCH_2P(O)(OR)_2 \xrightarrow{H_2O} (RO)_2P(O)CH_2C(O)H .$$

The ambiguous interaction between phosphorus pentachloride and enolic esters, shown by the studies of the same investigators, does not allow the synthesis of a wide variety of aldehydes by this procedure.

Unsaturated phosphorylated aldehydes have been obtained via the corresponding acetals [46]. The latter were synthesised from the products of the phosphorylation with phosphorus pentachloride of allyl ethers in accordance with the following scheme:

$$CH_2{=}CHCH_2OR + 2PCl_5 \rightarrow [\text{complex}] \xrightarrow{SO_2} Cl_2P(O)CH{=}CH{-}CH(OR)Cl \rightarrow \xrightarrow{R'ONa} (R'O)_2P(O)CH{=}CH{-}CH(OR)OR' \xrightarrow[(H^+)]{H_2O} [(R'O)_2P(O)CH{=}CH{-}C(O)H]$$

$$\rightarrow (R'O)_2P(O)CH(CH_3)CH(CH_2)CH(O)H \xrightarrow{C_6H_6} (R'O)_2P(O)CH(CH_3)CH_2 \xrightarrow{H_2NNHC_6H_3(NO_2)_2} (R'O)_2P(O)CH{=}CHCH{=}NNHC_6H_3(NO_2)_2 .$$

In view of their instability, phosphonoacroleins were not isolated in a free state and were identified only as their 2,4-dinitrophenylhydrazones. If the hydrolysis of the corresponding acetal is carried out in the presence of a conjugated diene, the phosphonoacrolein formed is involved in a Diels–Alder synthesis [46,47]. This reaction not only confirms the structure of the phosphonoacrolein but also constitutes a method for the synthesis of phosphorylated alicyclic aldehydes. Phosphonomethacrolein was obtained from methylallyl ether via the scheme described above [48] and, in contrast to its unsubstituted analogue, proved to be more stable and was isolated in a free state.

A method of synthesising phosphorylated diacetals based on the following general scheme has been developed in our laboratory: the phosphorus(III) acid chloride reacts with the acetal of glycolaldehyde to form the corresponding phosphorus(III) acid ester containing the acetal group in the ester moiety; the interaction of the latter via the Arbuzov reaction with the acetal of bromoacetaldehyde leads to the corresponding diacetals [49]:

$$ROPCl_2 + 2HOCH_2CH(OR')_2 \xrightarrow{Et_3N} ROP[OCH_2CH(OR')_2]_2 \rightarrow \xrightarrow{BrCH_2CH(OEt)_2} ROP(O)(OCH_2CH(OR')_2)(CH_2CH(OR)_2) .$$

In the products synthesised, one of the acetal groups is contained in the alkyl substituent linked to the phosphorus atom and the other is in the ester moiety.

Compounds containing the formyl group attached directly to the phosphorus atom are still unknown. Possibly they cannot exist at all. We believe that the structure of the product quoted by Isamu [50] is unlikely. On the other hand, acetals of similar aldehydes are readily available and can be obtained in two ways: by the condensation of the partial esters of phosphorus(III) acid with orthoformic esters [51]:

$$>POH + HC(OR)_3 \xrightarrow{t^\circ} >P(O)CH(OR)_2 + ROH$$

or by the interaction of the latter with phosphorus(III) acid chlorides [52,53]:

$$>PCl + HC(OR)_3 \rightarrow [>POR + ClCH(OR)_2] \rightarrow >P(O)CH(OR)_2 + RCl .$$

Satisfactory yields of phosphorylated formals are achieved by the first method only in the reaction with dialkyl phosphites; acid phosphonites and secondary phosphine oxides

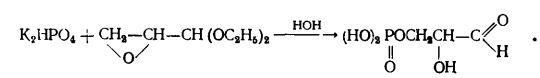
give extremely low yields of condensation products. The second method of synthesis—via phosphorus(III) acid chlorides—is more universal. The acetals of dimethylformamide (DMF) react with phosphorus(III) acid chlorides like orthoformic ester [54].

The hydrolysis of phosphonoformals does not lead to the corresponding aldehydes but involves the dissociation of the C–P bond [55] with formation of the initial dialkyl phosphite, alcohol, and alkyl formate.

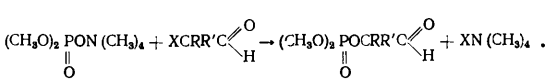
The structures of the phosphorylated aldehydes were confirmed in almost all cases by infrared spectroscopy and by the formation of 2,4-dinitrophenylhydrazones. In later investigations, NMR as well as infrared spectroscopy was employed.

Apart from the studies on phosphorylated aldehydes containing the formyl group in the substituent linked to the phosphorus atom by the C–P bond described above, mention has been made in the literature of compounds in which the formyl group is in the substituent linked to the phosphorus atom via a heteroatom (O, S, or N) and of phosphorus ylids and phosphonium salts. These studies on methods of synthesis cannot as yet be fitted into a definite system and therefore we shall confine ourselves to the enumeration of individual investigations in this field.

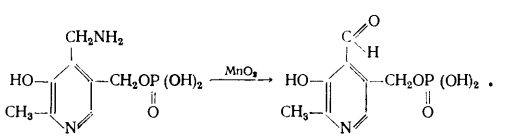
The interaction of the acetal of 2,3-epoxypropionaldehyde with dipotassium hydrogen phosphate followed by hydrolysis yielded glyceraldehyde phosphate [56]:



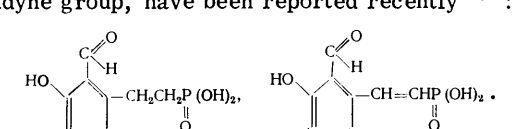
Another method of synthesising formyl-containing phosphates [57] consists in the interaction of the ammonium salts of phosphate esters with halogenoaldehydes:



Certain formyl-containing phosphates are interesting biologically active compounds. Pyridoxal phosphate [57-59], the synthesis of which involves the interaction of pyridoxamine with phosphoric acid followed by oxidation of the reaction product, is the most striking derivative of this kind:

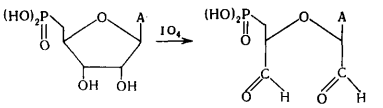


Phosphonic analogues of pyridoxal phosphate, in which the ester oxygen has been replaced by a methylene or methylidyne group, have been reported recently [60,61]:



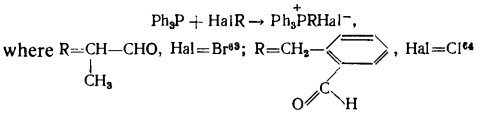
Their synthesis is based on the interaction of the corresponding pyridinealdehyde with phosphonate Wittig reagents, in particular with tetraethylmethylenediphosphonate. Esters of vinyl- and ethyl-phosphonic acids have been obtained by the oxidation of the hydroxymethylene group to the formyl group under mild conditions. The esters are hydrolysed by concentrated hydrochloric acid and phosphonic acid analogues of pyridoxal phosphate are isolated.

When adenosine monophosphate is oxidised by periodate, dialdehydes of the following type are formed [62]:



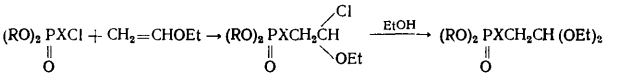
A = adenine residue

A series of phosphonium salts containing the aldehyde group are known [63,64]. Their synthesis is based on the interaction of triphenylphosphine with halogenoaldehydes:



Kirsanov and coworkers began the study of phosphazo-compounds with the aldehyde group in the aromatic ring, which are synthesised by the interaction of azidoaldehydes [65] or their oximes [66] with triphenylphosphine. In the latter case, the aldehyde was isolated by hydrolysing the oxime.

Acetals with the general formula $(RO)_2PXCH_2CH(OR')_2$ [67,68] where X = S or Se, are obtained according to the scheme



Acid hydrolysis of the acetal of the thio-derivative [67] led to the isolation of the corresponding aldehydes.

Several methods of synthesising aldehydes of the phosphorane type have been described, namely by the formylation of phosphinoalkylenes $Ph_3P{=}CH_2$ by *N*-formylimidazole [69] or ethyl formate [70] and also by the interaction of bromonitroethylenes with triphenylphosphine [71].

Compounds containing the formyl residue at a nitrogen atom linked to the phosphorus atom can be regarded as substituted formamides and are therefore not dealt with in the present review.

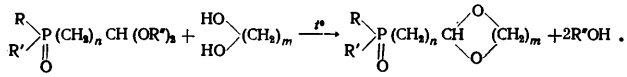
The foregoing discussion shows that many different types of synthesis of phosphorylated acetals and aldehydes have been described in the literature. The choice of a specific method for preparative purposes is determined mainly by the structure of the aldehyde to be synthesised and by the availability of the initial compounds. The advantages and disadvantages of individual methods have been stated in their discussion.

III. CHEMICAL PROPERTIES OF PHOSPHORYLATED ALDEHYDES

The chemical properties of phosphorylated aldehydes have been investigated much less than the methods of their synthesis. The limited number of studies in this field still precludes a broad general description of studies on the reactivity of compounds of this class and in the first place a description of the effects of electronic and steric factors on the course of nucleophilic addition reactions, which are most characteristic of the carbonyl group. Studies on keto-enol tautomerism of phosphorylated aldehydes, in which the mutual influence of the phosphorus-containing and formyl groups is clearly revealed, constitute an exception.

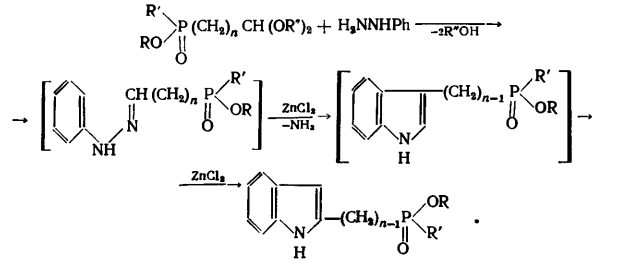
The first publications dealing with syntheses on the basis of phosphorylated aldehydes confirm their usefulness in this field. Certain reactions of phosphorylated aldehydes are described below. The most thoroughly investigated synthetic application of phosphorylated aldehydes is the synthesis of phosphorylated heterocyclic compounds with phosphorus in the side chain [72]. The first attempt to synthesise a phosphorylated aldehyde [1] was undertaken precisely with the aim of its subsequent employment to synthesise phosphorylated heterocycles. In many cases phosphorylated acetals were used successfully in the syntheses instead of phosphorylated aldehydes.

The reaction of phosphorylated acetals with diols yielded phosphorylated 1,3-dioxolanes [73], 1,3-dioxans [74], and polymethylene acetals [75]:



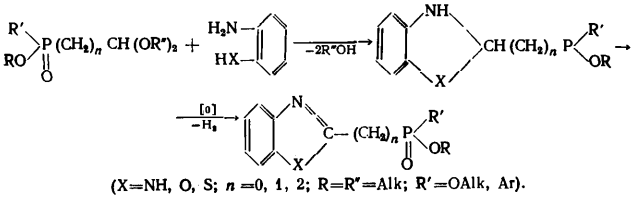
The reaction is carried out by heating equimolar amounts of the reactants with simultaneous distillation of the alcohol liberated. The phosphorylation of poly(vinyl alcohol) by phosphonoacetaldehyde can also be regarded as a transacetalisation reaction [76].

Phosphorylated acetals enter into a Fischer cyclisation reaction with arylhydrazines, forming phosphorylated indoles [5,77]:



It has been shown that the indoles phosphorylated in the 3-position, which are formed initially, isomerise to the 2-derivatives in the presence of an excess of zinc chloride.

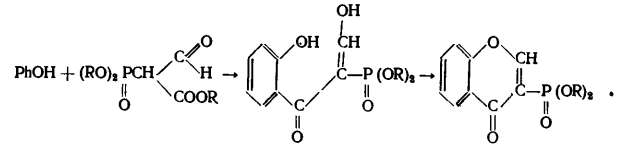
A wide range of phosphorylated heterocycles can also be obtained by the condensation of phosphorylated acetals with aromatic *ortho*-disubstituted compounds containing mobile hydrogen atoms, such as *o*-phenylenediamine, *o*-aminophenol, *o*-aminothiophenol, and others:



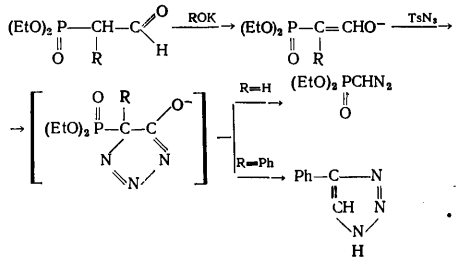
(X=NH, O, S; n =0, 1, 2; R=R″=Alk; R′=OAlk, Ar).

These reactions, which are common to the given classes of compounds, yielded respectively phosphorylated benzimidazoles [77,78], benzoxazoles [79], and benzothiazoles [80]. 2-Phosphorylated benzazoles are synthesised via a stage involving the formation of azolines [81]. The interaction of phosphorylated acetals with *o*-dihydroxy-derivatives of benzene and naphthalene resulting in the corresponding phosphorylated dioxoles takes place similarly [82]. Thus acetals of real phosphorylated aldehydes and derivatives known only in the acetal form (phosphorylated formals) have been used in the condensation reactions [77-82]. It has been found that, as the phosphorus-containing substituent moves further away from the acetal group, the rate of reaction increases, which can be accounted for by the decrease of the effect of the electron-accepting substituent on the mobility of the alkoxy-groups in the acetal moiety.

Substituted phosphorylated aldehydes also enter into a condensation reaction with monohydric phenols to form phosphorylated heterocycles [25]:

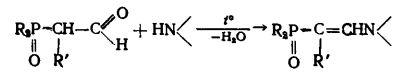


The ability of phosphorylated aldehydes to be converted comparatively readily into phosphorylated diazo-compounds greatly extends their synthetic possibilities, including the synthesis of heterocycles [83,84]:

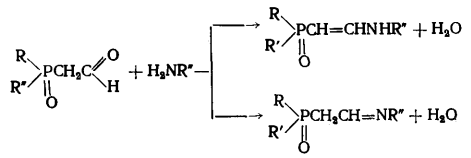


The free phosphonodiazomethane isolated [84] can be used for various organophosphorus syntheses.

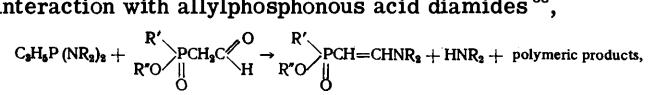
Phosphorylated enamines—a little known class of organophosphorus compounds—can also be obtained successfully from phosphorylated aldehydes. The interaction of equimolar amounts of the latter with cyclohexylamine in methanol [85] or with secondary aliphatic amines in toluene in the presence of catalytic amounts of toluene-*p*-sulphonic acid, accompanied by azeotropic distillation of water [86], gave satisfactory yields of phosphorylated enamines:



The interaction of phosphorylated aldehydes with primary amines leads to phosphorylated enamines, imines, or their mixtures depending on the structure of the amine employed [87]:

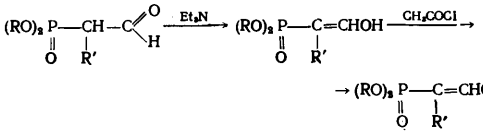


Virtually only enamines are formed when there is an electron-donating substituent at the nitrogen atom. When an electron-accepting substituent is present at the nitrogen atom, either a pure imine or a mixture of both products with the imine form predominating is formed. Whereas the direct interaction of secondary amines with phosphorylated aldehydes can involve either the keto- or the enolic form of the latter, the synthesis of phosphorylated enamines from the corresponding aldehydes via their interaction with allylphosphonous acid diamides [88],



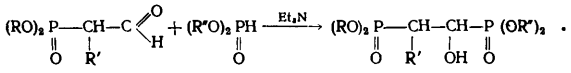
apparently involves the enolic form of the aldehydes.

Acylation of the enolic form of phosphorylated aldehydes by acetyl chloride in the presence of bases leads to β-acyloxyalkenylphosphonates [89]:



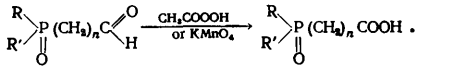
^{1}H NMR spectra have shown that the β-acyloxyvinylphosphonates, like the β-dialkylaminovinylphosphonates discussed above, have exclusively (or at least within the limits of the sensitivity of the ^{1}H NMR method) the *trans*-(P, O, or P, N) form. There are no specific data which would provide an answer to the question concerning the reason for the formation of only one geometrical isomer: either by the involvement in the reaction of only the *trans*-enolic form of the phosphorylated aldehyde or by the capacity of the *cis*-form of the corresponding derivative to isomerise readily under the reaction conditions to the energetically more favourable *trans*-form.

The extension of the familiar reactions of partial phosphorus(III) acid esters with aldehydes and ketones [90] to phosphorylated aldehydes leads to new possibilities in the synthesis of substituted ethylenediphosphonates [13,20]:

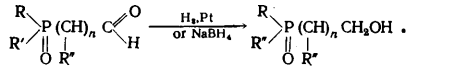


The reaction in the presence of a tertiary amine [13] or directly with dicyclohexyl phosphite salt [20] proceeds vigorously and reaches completion rapidly. On this basis, one may conclude that the aldehyde groups influenced by the electron-accepting phosphorus-containing substituent exhibit a fairly high electrophilic activity.

Phosphorylated aldehydes are oxidised by peracids [91] or by alkaline potassium permanganate [92] to the corresponding phosphorylated carboxylic acids:



The reduction of phosphorylated aldehydes over a platinum catalyst [27] or by sodium borohydride [93] leads to the corresponding hydroxy-derivatives in fairly high yields:



β-Aminoethylphosphonate has been obtained by the reduction of phosphonoacetaldehyde oxime in acetic anhydride [92].

Thus the data described show that the oxidation and reduction reactions of phosphorylated aldehydes and their derivatives can be used for preparative syntheses of organophosphorus compounds with functional groups.

The capacity of phosphorylated acroleins to undergo the Diels–Alder reaction [46,47] was mentioned above. The absence of a similar reaction involving phosphonomethacrolein has been explained [48] by the increased steric hindrance and by the electron-donating properties of the methyl groups, which reduce the electrophilicity of the C=C bond.

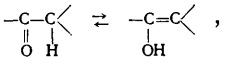
The diethylacetal of diethoxyphosphonoacetaldehyde has been used to synthesis olefins (via phosphonate carbanions). This acetal has been used successfully to synthesise cinnamaldehyde from benzaldehyde [94], but it did not react with steroid ketones [95].

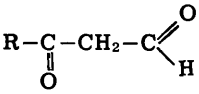
It has been noted [92] that, in an acid medium at an elevated temperature (90°C), phosphonoacetaldehyde decomposes with formation of acetaldehyde and inorganic phosphate. Possibly this constitutes one of the explanations of our earlier observation [2] that in the hydrolysis of phosphorylated acetals a high yield of aldehyde is achieved when volatile products and the excess volatile acid are removed from the hydrolysis product *in vacuo* before distillation. The high sensitivity of phosphorylated aldehydes to acids was also pointed out by Tavs [13]. On the other hand, a considerable excess of acid has been employed in many studies [19,20,23] involving the hydrolysis of phosphorylated enolic ethers without a significant decrease of the yield of the phosphorylated aldehyde.

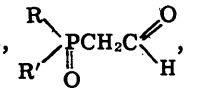
It follows from the data discussed that the properties characteristic of the aldehyde group are largely retained in phosphorylated aldehydes. This suggests that in future all the potentialities of the aldehyde group will be widely employed in organophosphorus synthesis.

IV. THE KETO–ENOL TAUTOMERISM OF PHOSPHORYLATED ALDEHYDES

The keto–enol tautomerism, involving the characteristic irreversible interconversion



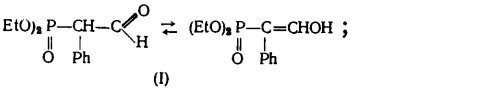
is very common and has been thoroughly investigated in organic chemistry. Mainly substances with two carbonyl groups separated by a methylene link were investigated in this field: β-diketones and β-ketoacid and malonic acid esters (β-dicarbonyl compounds) [96]. β-Ketoaldehydes with an unsubstituted methylene group,  , have not been investigated in this connection in view of their low stability [97]. There are only isolated data [98,99] showing a somewhat higher stability of their keto-enol form. For further investigation of such tautomerism, it was of great interest to study other chemical series with structures close to that of β-ketoaldehydes.

Phosphorylated aldehydes are one such class of compounds. These include primarily phosphorus analogues of β-dicarbonyl compounds,  , in which the C=O group has been replaced by the P=O group. The considerable similarity between the structures and properties of the two classes of compounds has been established for a long time and has been the subject of numerous investigations [32,100–102].

On the basis of these considerations, it was to be expected that α-phosphorylated aldehydes should exhibit keto–enol tautomerism. Presumably, apart from the principal external and structural factors determining the tautomeric equilibrium of β-dicarbonyl compounds, the P=O group also plays a significant role in phosphorylated aldehydes. It can exert an influence via the formation of hydrogen-bonded complexes with the hydrogen atom of the OH group of the enolic forms (which are more stable than in the case of the C=O group [103]) and via the involvement of the 3*d* orbitals of phosphorus in conjugation with the double bond of the enolic forms. Moreover, one cannot fail to

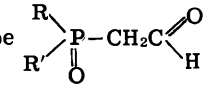
take into account the possible steric factors due to the larger bulk of the P=O group compared with that of the C=O group.

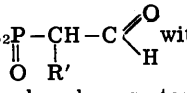
Indeed, in 1960 Tammelin and Fagalind [27] described the tautomeric properties of 2-diethoxyphosphonyl-2-phenylacetaldehyde (I), which they obtained,



(I)

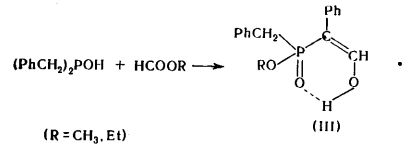
they resemble those of ethyl phenylformylacetate (II). Comparison of the infrared spectra and the dissociation constants of compounds (I) and (II) and also the spectrophotometric determination [on the basis of the colour of the complex with iron(III) chloride] of the keto–enol equilibrium constant and the rate of enolisation of compound (I) led the authors [104] to the conclusion that compounds (I) and (II) exist only in the keto- and *cis*-enolic forms in carbon tetrachloride and isopropyl alcohol solutions and that the *trans*-form is absent from such solutions. The infrared spectra of compound (I) showed the absorption bands of the OH group involved in an intramolecular hydrogen bond. At the same time the vibration frequency of the P=O group was displaced towards longer wavelengths, which indicated the formation of a hydrogen bond between them, while the enolisation of the phosphoryl group was not observed. The dissociation constants of compounds (I) and (II) were found to be very similar (pK_a = 7.09 and 7.21 respectively).

In subsequent studies dealing with the keto–enol tautomerism of α-phosphorylated aldehydes, two main trends were established. On the one hand, aldehydes without a second substituent at the α-carbon atom of the type  were investigated and the influence of substituents at the phosphorus atom on the position of the keto–enol equilibrium was elucidated. These investigations make it possible to estimate the intrinsic effect of the  groups, since in these cases it is not masked by the superposition of any other effect of substituents in the methylene group.

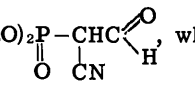
On the other hand, a study was made of the effect of substituents at the carbon atom in α-substituted aldehydes of the type  with retention of the same groups at the phosphorus atom. The substituents R′ were chosen mainly so that they could enter into conjugation with the π-electrons of the double bonds of the enols. At the same time, the introduction of the α-substituent can alter the molecular geometry, hindering the reverse transition into the keto-form, and hence can increase the general tendency towards enolisation. With this aim in view, groups possessing a considerable resonance component σ_R (CN, CH_3CO, COOR), together with a high negative inductive effect ($-I$), were employed as substituents in the first place. They make it possible to shift the equilibrium almost completely towards the enolic form. Next, substituents with lower values of σ^* (C_6H_5, Cl, Br) were introduced, and finally substituents exhibiting a positive inductive effect. In all these cases, the equilibrium was displaced towards the enolic form. The fact that substituents with opposite inductive effects (halogens [29] and alkyl groups [21]) caused an unambiguous shift of the equilibrium towards the enol cannot as yet be satisfactorily accounted for without additional investigations.

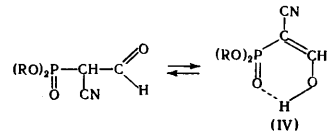
Thus, in studies of the second type, a decisive influence is attributed to the nature of the substituents at the α-carbon atom. The phosphoryl group influences the nature of the enolisation reaction (*cis*–*trans*-enolisation) and causes a slight shift of the equilibria. Naturally, particular investigations cannot always be definitely assigned to a particular type, since the data accumulated suggest quite clearly that the effect of the substituents at both the α-carbon atom and at the phosphorus atom is fairly important. In view of these findings, in later studies investigators attempted to take into account the overall effect of all the substituents present in the molecule. Chronologically, it is more convenient to consider initially the keto–enol tautomerism of substituted phosphorylated acetaldehydes.

In a further development of studies mentioned above [27,104], Arbuzov and coworkers [31] attempted to synthesise phosphorus-containing dialdehydes. However, they isolated alkoxybenzylphosphinylphenylacetaldehydes in the crystalline enolic forms (III) with stable cisoid configurations, which are sparingly soluble in organic solvents:



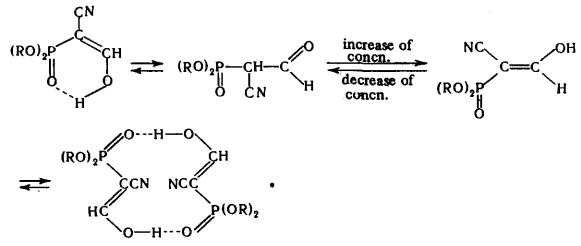
(III)

Kirilov and Petrov [28] investigated the tautomerisms of cyanoaldehydes of the type  , where R = C_2H_5, n-C_3H_7, or n-C_4H_9, by infrared spectroscopy and by titration. However, the classical bromometric method proved to be unsuitable in view of the sensitivity of the aldehyde groups to bromine. A method involving the acidimetric titration of aqueous solutions of aldehydes with 0.01 M NaOH revealed the presence of up to 98% of the enolic form. On the basis of the literature data and the frequency shift of the OH and P=O groups in the infrared spectra, the authors suggest that a cisoid structure (IV) with an intramolecular hydrogen bond is characteristic of the enolic form and they explain the high stability of this bond by the considerable polarity of the P=O group:



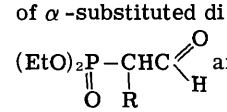
(IV)

The study of the infrared spectra of solutions of the aldehydes in carbon tetrachloride (at concentrations of 0.4 and 3.63%) led to the hypothesis that new enolic forms, namely the dimeric forms (V) and polymeric forms with an intermolecular hydrogen bond and involving *trans*-enols, appear in more concentrated solutions:

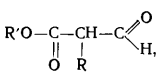


The dimeric structure is thought to be confirmed by the characteristic increase of the intensity of the absorption bands associated with the deformation vibrations of the bound OH group, with the concentration of the solution.

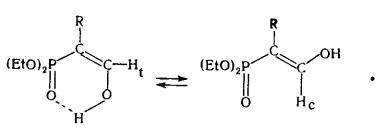
In a series of interesting studies, Kabachnik, Ioffe, and others [26,29,30,105-109] investigated by ^{1}H NMR the enolisation of α-substituted diethoxyphosphonoacetaldehydes



and compared it with the tendency towards enolisation in the corresponding substituted formylacetic esters:

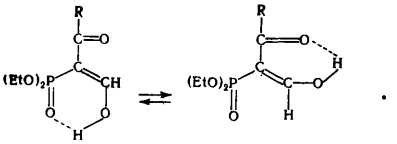


where R = CN, COOEt,[26] Ph, Cl, Br, or CH_3CO.[29] Particular attention was devoted to the elucidation of the nature of the hydrogen bonds. One should bear in mind that, owing to the lower thermodynamic stability of the *trans*-enolic form compared with the *cis*-enolic form [110], the *trans*-enolisation of open-chain formyl derivatives takes place extremely rarely and only under conditions such that structural factors or the solvent cause an additional stabilisation of the *trans*-form. One should also mention that hitherto there have been no reliably established instances of the *trans*-enolisation of open-chain β-dicarbonyl compounds with the exception of a small number of formyl derivatives [111,112]. The assignment of the tautomeric enolic forms to the *cis*-(VI) or *trans*-series (VII) was based on the vinyl proton signals in the ^{1}H NMR spectra. Integration of the signals made it possible to estimate the contents of the *cis*- and *trans*-isomers of the enolic forms relative to the P=O and OH groups:



cis (VI) *trans* (VII)

In addition, in acetyl- and ethoxycarbonyl derivatives there is a possibility of competition between two *cis*-enolic forms with chelation in different directions. Thus an intramolecular hydrogen bond can be formed with both C=O [formula (VIII)] and P=O groups [formula (IX)]:



P-*cis* (VIII) C-*cis* (VIII)

(R = CH_3, OEt)

The results of the investigations showed that, in the case of the ethoxycarbonyl derivative, the P-*cis*-form (VIII) is mainly involved in the equilibrium owing to the higher basicity of the P=O group compared with that of the carbonyl group. On the other hand, in the acetyl derivative the C-*cis*-form is dominant, probably due to the opposite changes in the basicities of the P=O and C=O groups. This enabled the authors to arrange the hydrogen bond acceptors in the following series in terms of their capacity for chelate-formation with the hydroxy-methylene group:

$$CH_3CO > (EtO)_2P(O) > COOEt$$

Determination of the proportions of the tautomeric forms in solvents of different polarities (carbon tetrachloride, dioxan, acetonitrile, and nitromethane) showed that, in solutions of phosphonic and carboxylic acids containing the CN, CH_3CO, and COOEt groups as α-substituents, the keto-form is absent (Table 1). This finding is probably related to the high acidity of the CH protons (Table 2) due to the appreciable inductive and mesomeric effect of the α-substituents.

According to the authors, the capacity for *trans*-enolisation is determined not so much by the steric effects as by the polar effects of the α-substituents. Thus, in acetonitrile esters containing chlorine and bromine exist in the *trans*-enolic and keto-forms but not in the *cis*-form. This phenomenon has been attributed to the inductive effect of the halogen atoms. The latter decrease the basicity of the P=O and C=O groups and reduce the energy of the hydrogen bond with a corresponding destabilisation of the pseudoaromatic ring of the *cis*-enolic form. On the other hand, in both acetonitrile and nitromethane the enolisation of carboxylic and phosphonic acids is similar, while in

Table 1. The content of the different forms (%) in solutions of diethyl formylmethylphosphonates and formylacetic esters [29].

R	RCH(CHO)COOEt									RCH(CHO)P(O)(OEt)$_2$								
	solvent									solvent								
	CCl_4			dioxan			CH_3CN			CCl_4			dioxan			CH_3CN		
	C	T	K	C	T	K	C	T	K	C	T	K	C	T	K	C	T	K
Ph	95	—	5*	92	—	8	90	—	10	85	—	15	95	—	5	93	—	7	89	—	11	85	—	15
Cl	10	80	10	16	70	14	—	80	20	—	75	25	—	82	18	—	73	27	—	67	33	—	62	38
Br	—	—	—	—	90	10	—	86	14	—	84	16	—	70	30	—	57	43	—	50	50	—	45	55
CN	—	—	—	60	40	—	52	48	—	16	84	—	46	54	—	37	63	—	31	69	—	14	86	—
CH_3CO	67	33	—	67	33	—	75	25	—	—	—	—	50	50	—	50	50	—	70	30	—	80	20	—
COOEt	100	—	—	—	—	—	—	—	—	—	—	—	81	19	—	84	16	—	74	26	—	73	27	—

C = *cis*-, T = *trans*-, K = keto.

*In $CDCl_3$.

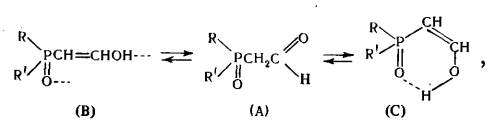
carbon tetrachloride and in dioxan differences are observed. For example, all three forms of chloroformylacetic ester are present in equilibrium, while the *cis*-enolic form of its phosphonic analogue is absent. Moreover, it has been shown that the *trans*-enolic form which predominates in the equilibrium is stabilised by intermolecular hydrogen bonds. In order to find the degree of association of the molecules, their molecular weights in benzene, dioxan, and acetonitrile were determined. It was discovered that carboxylic acid derivatives are monomeric, while phosphonic acid derivatives are associated in benzene but are converted into monomers during ebullioscopic determinations in acetonitrile. In the latter case, intermolecular hydrogen bonds are ruptured at the boiling point of the solvent. The results provide additional evidence in support of the above hypothesis concerning the intermolecular association of the enolic forms in solution, which stabilises them. The observations are also supported by infrared spectroscopic data [108].

Table 2. The pK_a values in water at 20°C. [29,109]

Compound	pK_a	Compound	pK_a
PhCH (CHO) COOEt	7.09	NCCH (CHO) COOEt	2.04
PhCH (CHO) P (O) $(OEt)_2$	7.21	NCCH (CHO) P (O) $(OEt)_2$	2.00
ClCH (CHO) COOEt	6.30	EtOOCCH (CHO) P (O) $(OEt)_2$	4.09
ClCH (CHO) P (O) $(OEt)_2$	6.11	CH_3COCH (CHO) P (O) $(OEt)_2$	3.68
BrCH (CHO) P (O) $(OEt)_2$	6.14	EtOOCCH (CHO) P (O) *n*-Bu_2	6.40

To confirm the dependence of the nature of the enolisation on the basicity of the C=O and P=O groups, a study was made [30] of the compounds n-Bu_2P(O)CH(R)CHO (R = COOEt or $COCH_3$). In contrast to the diethoxyphosphono-derivatives with the general formula $(EtO)_2$P(O)CH(R)CHO discussed previously, in the present case the enolic forms present in the equilibrium solution in acetonitrile have only the *cis*-configuration. They are stabilised by an intramolecular hydrogen bond, since the n-Bu_2P(O) group becomes a more basic chelating centre. It is extremely difficult to generalise these results and to find general relations governing the enolisation of phosphonoacetaldehydes, since in this case the overall effects of the α-substituents and the R(R′)P(O) groups operates. A characteristic pattern may be observed for each substituent and one of the above effects may become of primary importance if it is sufficiently powerful, as can be seen from halogeno- and cyano-derivatives. On the other hand, the interaction of all the effects enumerated creates different nuances in the type of enolisation which is a highly refined phenomenon [109].

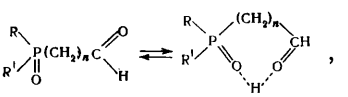
Therefore the study of unsubstituted phosphorylated aldehydes, where the complicating effect of α-substituents is removed and it is possible to follow the effect of the R(R′)P(O) group alone, is of special interest. The keto–enol tautomerism of unsubstituted phosphorylated aldehydes has been studied in a number of investigations [6-8,113-115]. In their approach to the solution of the problem of the relative amounts of tautomers in aldehydes of different classes of organophosphorus compounds (phosphonates, phosphinates, and phosphine oxides), Razumov and coworkers employed infrared, ^{1}H NMR, and ^{31}P NMR spectroscopic methods and to some extent polarography [6-8,113-115]. The following keto–enol equilibrium is observed in series of unsubstituted phosphorylated aldehydes:



(B) (A) (C)

where R = OAlk, C_2H_5, C_3H_5, or C_6H_5 and R′ = OAlk, C_2H_5, or C_6H_5.

Apart from the usual external factors (medium, temperature, and concentration), the equilibrium depends directly on the nature of the R(R′)P(O) group. In polarographic studies of the behaviour of phosphorylated acetaldehydes and propionaldehydes in neutral, alkaline, and acid aqueous solutions, it was found in the first place that their polarographic activity is due to the aldehyde group and not the phosphoryl group, since the latter is not reduced at the dropping mercury electrode. It was discovered that in a neutral aqueous medium aldehydes exist in the keto-form in equilibrium with the hydrated form:



where R = C_2H_5, C_6H_5, p-ClC_6H_4, p-$CH_3C_6H_4$, or OC_2H_5 and R′ = OC_2H_5.

The polarographically active form amounts to 11–12% for phosphinylacetaldehydes and 20–22% for phosphinylpropionaldehydes. In acid solutions, the equilibrium is displaced towards the enol and in alkaline solutions the enolic form is not detected, since it probably exists in the form of a polarographically non-reducible anion. A study was also made of the influence of the group R on the capacity of the aldehyde group to be hydrated and on the tendency towards enolisation. In phosphinylacetaldehydes, the effect is shown to a much greater extent than in phosphinylpropionaldehydes, but the effect is of the same type [113,114].

The employment of infrared and NMR spectroscopic methods in the study of the keto–enol equilibrium led to the discovery of many interesting relations governing the processes. Experiments were performed for many compounds of the series mentioned above. In each series ethoxy- and isopropoxy-groups were always present, which made it possible to follow the effect of only one substituent at the phosphorus atom. The study of the dependence of the position of the keto–enol equilibrium on the nature of the substituent showed that it is determined mainly by the basicity of the P=O group, which limits its capacity to form hydrogen bonds stabilising the enolic forms, and to a lesser extent by steric factors.

The basicity of the P=O group as a function of the nature of the substituent can be assessed from the chemical shifts $\delta^{31}P$ of the phosphorus nuclei, the energy of the π bond, and the shifts of the OH frequencies of the enolic forms in the infrared spectra. The latter also make it possible to establish that the acidity of the enolic forms is constant ($pK_a = 7.5 \pm 0.03$)‡ within the limits of the accuracy with which $\Delta\nu$(OH) is measured for the series investigated. The authors observed that, with increase of the basicity of the P=O group and the consequent increase of the hydrogen bond energy, there is a successive shift of the position of the keto–enol equilibrium towards the enol (Table 3). The aldehydes investigated can be arranged in the following sequence in terms of increasing amounts of the enolic form:

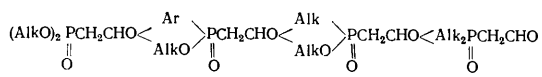
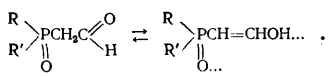


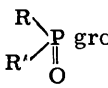
Table 3. The keto–enol equilibrium constants, free energies, π-bond energies, hydroxy-group frequency shifts, and the chemical shifts of the phosphorus nuclei of phosphorylated acetaldehydes[8]:

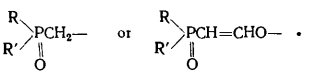


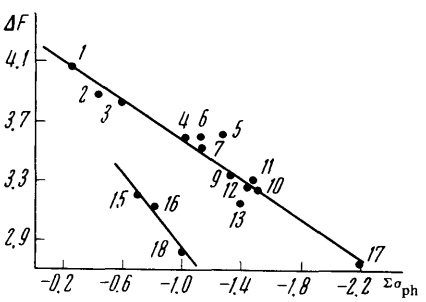
No.	R	R′	10^3K_e	ΔF	E_π, kcal mole^{-1}	$\Delta\nu$(OH) cm^{-1}	10^3K_e CCl$_4$ 0.2 M	CCl$_4$ 0.05 M	dioxan 0.1 M	hexane 0.1 M	δ^{31}P, p.p.m.
1	CH_3O	CH_3O	1.09	4.09	67.3	220					
2	EtO	C_2H_5O	1.475	3.88	66.9	260	1.06	0.117			−20
3	*i*-C_3H_7O	*i*-C_3H_7O	1.585	3.84	66.2	270	1.15	—			−18
4	C_3H_5	EtO	2.41	3.59	63.9	340	1.91	—			−44
5	C_3H_5	*n*-C_4H_9O	2.28	3.63	64.0	340	1.54	0.07	0.1	1.91	−43
6	C_3H_5	*i*-C_4H_9O	2.20	3.64	63.78	—	1.33	0.03	0.04	—	—
7	C_3H_5	*i*-C_5H_7O	2.75	3.52	63.8	350	2.22	—			−40
8	C_3H_5	s-C_4H_9O	3.14	3.46	63.7	360	1.75	0.12	0.05	1.93	—
9	Et	EtO	3.61	3.36	62.2	385	2.102	0.132			−49
10	Et	*n*-C_4H_9O	4.01	3.28	62.2	390	1.02	—	0.29	1.90	−49.5
11	Et	*n*-C_5H_7O	4.34	3.26	62.2	390	2.39	0.147			−48.5
12	Et	*i*-C_4H_9O	4.23	3.24	61.7	393	2.42	1.82	1.03	2.86	−47.7
13	Et	*i*-C_5H_7O	5.15	3.15	61.6	397	2.98	0.197			−47.5
14	Et	s-C_4H_9O	6.36	3.02	59.9	430	4.91	3.81	0.83	2.16	−46
15	Ph	EtO	4.52	3.21	65.2	300	3.38				−34
16	Ph	*i*-C_5H_7O	5.46	3.12	64.2	320	3.31				−32
17	Et	Et	12.34	2.74	56.3	470					
18	Ph	Ph	8.9	2.82	57.5	420					

Table 3 shows that the keto–enol equilibrium constant, the basicity of the P=O group, and the charge on the phosphorus atom increase and the free energy and the π-bond energy decrease with increase of the positive inductive effect of the substituents and with decrease of the p_π–d_π conjugation of the phosphorus atom with the surrounding atoms. The experimental ΔF are satisfactorily correlated with Kabachnik's constants for the substituents[116] (Fig. 1), i.e. the keto–enol equilibrium constant is directly related to the basicity of the P=O group and thereby demonstrates unambiguously the role of the latter as the decisive factor in this equilibrium.

‡ pK_a was determined from the $\Delta\nu$(OH) shift in triethylamine.

It follows from the foregoing that the transmission of the influence of the  group takes place via a hydrogen-bonded complex and not via the system





Variation of ΔF with $\Sigma\sigma_{ph}$ after Kabachnik; the numbers of the points in the graph correspond to the numbers of the compound in Table 3.

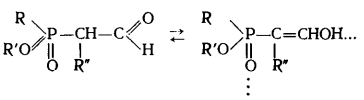
Structures with intramolecular (*cis*-) and intermolecular (*trans*-) hydrogen bonds (structures B and C) are characteristic of the enolic forms of phosphorylated acetaldehydes. The study of the nature of the hydrogen bonds by infrared spectroscopy showed that the undiluted compounds have structures with both configurations (B and C). For all the aldehydes investigated and the substances with the isopropoxy-group, the intramolecular hydrogen bond is stronger and the equilibrium constant is higher than for ethoxy derivatives. These findings can probably be accounted for not only by the higher basicity of the P=O group in the former compounds but also by the steric effect of the isopropoxy-residue, which leads to the proximity of the P=O and OH groups in the *cis*-positions of the enolic form (which can be seen also from the Stuart–Briegleb models).

To elucidate the type of enolisation of aldehydes, a study was made of their behaviour both in solvents with different polarities and basicities and as a function of temperature. Interesting observations were made. In non-polar solvents (carbon tetrachloride, dioxan, and hexane; in the last solvent only the aldehydes with high molecular weights are soluble), the equilibrium is displaced towards the keto-form, i.e. in a direction opposite to that for β-dicarbonyl compounds and phosphorylated ketones. Examination of the concentration variation in carbon tetrachloride (0.5, 0.05, and 0.005 M solutions) indicated a stabilisation of the enolic forms mainly by intermolecular association. On the other hand, in solutions the intermolecular hydrogen bonds present in the undiluted compounds and in more concentrated solutions are ruptured. Hence the presence of only one keto-form in 0.005 M solutions (Table 3, compounds 3, 4, 7, 10, 15, and 16) and of an insignificant amount of the *cis*-enolic form in certain cases become understandable.

When aldehydes are dissolved in a highly basic solvent (triethylamine), the situation changes. Here the equilibrium is displaced in the opposite direction—towards the enol with formation of a chelated structure involving powerful hydrogen bonds.

The study of the temperature variation of the keto–enol equilibrium showed that a change in temperature has a significant influence on the relative amounts of the forms [115]. With increase of temperature from 11° to 100°C, there is initially a transition from the *trans*-enol to the keto-form. This shift of the equilibrium is accompanied by a decrease of the content of the *trans*-enolic form and takes place up to temperatures in the range 50–75°C depending on the nature of the substituent at the phosphorus atom. A further increase of temperature to 95–100°C causes a shift towards the *cis*-enolic form.

Table 4. Keto–enol equilibrium constants, enthalpies, and entropies of phosphorylated aldehydes [115]:



R	R′	R″	10^3K_1, temperature, °C							ΔH	ΔS	10^2K_2 (*cis* ⇌ *trans*) at 25°C
			11	25	35	50	60	75	95			
Et	EtO	H	—	3.50	—	2.51	—	2.97	4.65	9.06	19.1	1.26
Et	*n*-C_5H_7O	H	6.36	5.02	4.30	3.68	3.60	3.85	6.02	8.88	19.2	1.22
Et	*s*-BuO	H	10.6	7.78	6.20	4.48	4.32	3.63	5.04	9.72	23.0	0.96
Ph	EtO	H	5.44	4.71	4.45	3 97	3.86	3.88	4.21	7.84	13.7	—
C_6H_5	EtO	H	3.47	2.77	2.40	1.95	1.87	1.78	2.48	9.16	18.9	—
EtO	EtO	H	2.33	1.74	1.6	1.5	1.72	2.06	3.2	8.84	17.5	2.78
EtO	EtO	CH_3	100	3.33	—	15.1	14.0	7.78	5.16	10.92	29.8	—
EtO	EtO	Et	31.7	16.0	—	11.8	6.2	4.27	2.5	10.95	28.5	—

The study of the concentration and temperature variation of phosphorylated aldehydes containing an alkyl substituent in the methylene unit, $(C_2H_5O)_2P(O)CHRCHO$ ($R = CH_3$ or C_2H_5), showed that their enolisation has other characteristics (Table 4). Then, whereas in the undiluted state at 20°C they exist in the keto- and *trans*-enolic form (33 and 67% respectively for $R = CH_3$ and 25 and 75% respectively for $R = C_2H_5$), on dilution with carbon tetrachloride (0.05 and 0.005 M solutions) as well as on raising the temperature to 100°C, they are converted from the *trans*-enolic form into the keto-form alone (75 and 25% for $R = CH_3$ and 80 and 20% for $R = C_2H_5$).

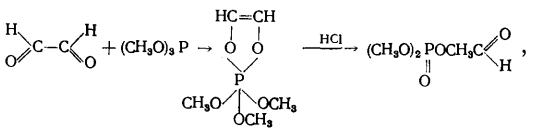
Thus the study of the tautomerism of phosphorylated aldehydes has led to the discovery of definite characteristics in their behaviour, which distinguish them from β-dicarbonyl compounds. These are as follows: firstly, α-phosphorylated aldehydes unsubstituted in the methylene group are stable keto–enol systems whose keto–enol equilibrium may be investigated; secondly, phosphorylated aldehydes are some of the few open-chain compounds capable of both *cis*- and *trans*-enolisation.

ADDENDUM

To make the review complete, mention must be made of a number of studies published recently when the manuscript of the review was with the editors. In addition to studies on the interaction of phosphorus(III) acid esters with the acetals of halogenoaldehydes, considered at the beginning of the review, Reichel and Jahns [117] examined the interaction of triethyl phosphite with the acetal of α-bromopropionaldehyde followed by hydrolysis of the Arbuzov reaction product to α-phosphonopropionaldehyde. In a continuation of the study reported previously [63], Reichel and Jahns [117] carried out a detailed synthesis of an aldehyde with a phosphonium structure.

Continuing their earlier investigations [54,55], Gross and Costisella [118] obtained data for the reactivities of phosphonoformals.

In addition to the earlier study by Ramirez et al. [119], who described the synthesis of aldophosphates according to the scheme



Kraus and Stürtz [120] extended the range of α-aldophosphates obtained by the method described above [57].

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Kirov Kazan Institute of
Chemical Engineering

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Cardopolymers (Loop Polymers)

S.V.Vinogradova and Ya.S.Vygodskii

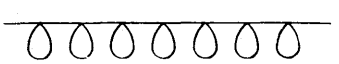
Polymers containing bulky side groups linked in ring form to the main chain are distinguished by a specific set of properties (cardopolymers). The review deals with the characteristics of the synthesis and with the physicochemical properties of cardopolycarbonates, cardopolyarylates, cardopolyamides, cardopolyimides, cardopoly-1,3,4-oxadiazoles, carbonchain cardopolymers, etc. The bibliography includes 232 references.

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I. INTRODUCTION

The set of physicochemical properties of polymers is in many ways determined by their chemical structure. Recently studies have been made in the field of polymers containing in the repeat units of the chain at least one element entering into the composition of a cyclic side group. It has been suggested[1] that such polymers be called cardopolymers from the latin word "cardo" (loop), since such groups can be regarded as loops in relation to the main chain of the macromolecule:



Naturally the properties of cardopolymers are influenced also by the structure of the main polymer chain. However, the presence in various types of heterochain and carbonchain polymers of cardo-groups imparts to them specific properties: a combination of enhanced heat resistance with excellent solubility, which is particularly important for rigid-chain aromatic heterocyclic polymers.

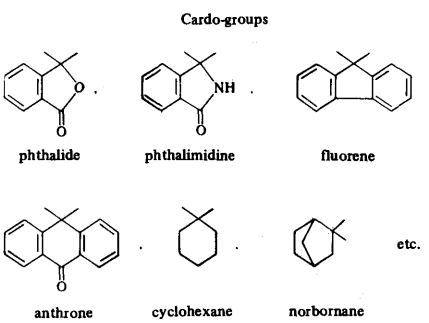
As early as the 1930's, Wagner[2] mentioned in his list of different initial compounds (diols) the possibility of employing phenolphthalein for the synthesis of polyesters. Data concerning the synthesis of resin-like products of complex composition from phenolphthalein were published in a number of reports[3-5].

A few of the early studies dealt with the products of the condensation of formaldehyde and phenolphthalein[6-10]. In 1946 a report was published on the synthesis of alkyd polymers of fluorescein and phenolphthalein[11] and two years later polymers were obtained by the polymerisation of diallylphenolphthalein dicarbonate[12]. Later data were published on the semiconductor properties of polymers prepared by heating phenolphthalein with $ZnCl_2$ at 256° and 306°C[13] and also on the epoxy-polymers based on phenolphthalein[14-18].

A characteristic feature of the above investigations is that phenolphthalein—the starting material for the synthesis of particular polymers—was used as a member of the enormous class of diols without taking into account its specific contribution to the properties of the polymer.

Systematic studies on cardopolymers as such probably began with the synthesis of high-molecular-weight polyarylates from phenolphthalein and various dicarboxylic acids in 1961 when, essentially for the first time, attention was turned to the specific contribution of the phthalide cardo-group to the formation of the set of properties of heterochain polymers[19,20].

So far numerous cardopolymers with ester, amide, imide, 1,3,4-oxadiazole, ether, etc. groups have been synthesised:



The introduction of cardo-groups into polyesters, polyethers, aromatic polyamides, heterocyclic polymers[21-25], and carbonchain polymers imparted to them many specific properties and made it possible to investigate characteristics which could not be estimated using polymers without such groups. In recent years the manufacture of first examples of cardopolymers (cardopolyarylates) has begun in the USSR on an experimental industrial scale.

Among the monomers with cardo-groups, perhaps only phenolphthalein [3,3-bis-(*p*-hydroxyphenyl)phthalide] is an industrial product employed in analytical chemistry and as a medicinal preparation. Other bi- or poly-functional compounds of the cardo-type have been studied much less, and frequently the information about them (before their employment in the synthesis of polymers) was restricted to one or two reports. Many cardomonomers were altogether unknown previously and were synthesised specially for the preparation of cardopolymers, for example 9,9-bis-(*p*-carboxyphenyl)-10-anthrone[26], the dianhydride of 3,3-bis-(3′,4′-dicarboxyphenyl)phthalide[27], and 2-(β-hydroxyethyl)-3,3-bis-(*p*-hydroxyphenyl)phthalimidine[28].

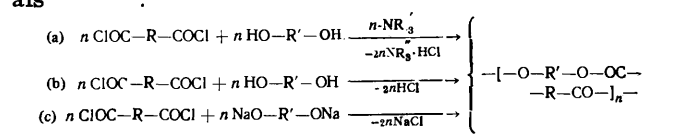
II. SYNTHESIS

The usual methods for the formation of polymers of a particular type are used as a rule to synthesise cardopolymers. Therefore in the present review attention has been

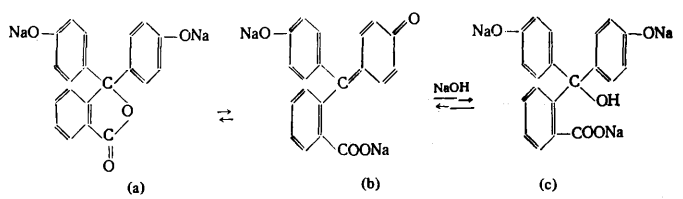
concentrated on those characteristics of the synthesis which are due to the specific features of the structure and behaviour of cardomonomers and cardopolymers. In addition certain general characteristics of the synthesis of the polymers of various classes have been traced using cardopolymers as an example and phenomena useful for the understanding of the reaction mechanism have been discovered; these findings have also been reflected in the review.

1. Bisphenol Polyesters

Bisphenol polyesters are obtained nowadays with the aid of different types of non-equilibrium polycondensations such as (a) low-temperature (acceptor-catalytic) polycondensation, (b) high-temperature polycondensation in solution, and (c) interfacial polycondensation using dicarboxylic acid chlorides and bisphenols as the starting materials[2,25,29-32]:



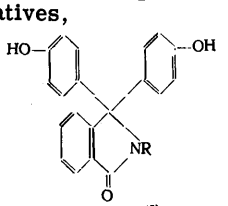
All these methods are also applicable to the preparation of cardopolyarylates. In many cases, when these polymers are synthesised by interfacial polycondensation, account must be taken of the specific features of the behaviour of cardomonomers such as phenolphthalein in aqueous alkaline media. The structure of phenolphthalein in an aqueous alkaline solution is known to depend on the amount of alkali present:



The formation of polyarylates without quinonoid structures in the interfacial polycondensation of phenolphthalein and dicarboxylic acid chlorides shows that a rearrangement or a shift of equilibrium between forms (B) and (A) takes place during the reaction and leads to the retention of the lactone ring in phenolphthalein[25,33,34].

The phthalide structure is characteristic of the glycidyl ether of phenolphthalein[35], which is formed in an alkaline medium, and of aromatic phenolphthalein polyethers obtained by the nucleophilic substitution of activated halogen-containing aromatic compounds[36,37]. The existence of cardobisphenols such as fluorescein or phenolsulphophthalein in the form of a mixture of isomers (in the quinonoid and lactone forms) even in a neutral medium hinders the synthesis of high-molecular-weight polymers based on them.

The replacement of phthalide derivatives by phthalimidine derivatives,



(R=H; Ph, ETOH etc.).

(I)

which do not undergo changes in an alkaline medium associated with formation of a quinonoid structure, makes it possible to synthesise high-molecular-weight polyarylates by interfacial polycondensation under the usual conditions[38]. One should only note that in the interfacial polycondensation of 2-(β-hydroxyethyl)-3,3-bis-(*p*-hydroxyphenyl)phthalimidine and isophthalic or terephthalic acid chlorides[39] in the presence of more than two moles of alkali, not only the phenolic but also the alcoholic hydroxyl is acylated, which leads to the formation of a cross-linked polymer.

Cardopolyarylates are usually synthesised by acceptor-catalytic polycondensation whereby it is possible to obtain high-molecular-weight polymers under mild conditions in a short time[25,39,40,41]. Much attention has been devoted to the study of the mechanism and characteristics of this process[31,32,40-47]. In contrast to interfacial polycondensation, where the behaviour of phenolphthalein is unusual, in acceptor-catalytic polycondensation in anhydrous solvents the structure of phenolphthalein does not change even in the presence of highly basic tertiary amines.

The greatest number of cardopolyarylates have been synthesised by the high-temperature polycondensation of dicarboxylic acid chlorides and bisphenols in organic solvents. The kinetics of this reaction have been investigated for the interaction of terephthalic acid chloride and 9,9-bis-(*p*-hydroxyphenyl)fluorene and other polycyclic bisphenols, which led to the suggestion of an ionic mechanism for this reaction, including the formation of an acylium ion[48,49]. Cardopolyarylates are synthesised in ditolylmethane[19,20], sovol[50-56] (a mixture of tetra- and pentachlorobiphenyls), α-chloronaphthalene[56], *o*-dichlorobenzene[57], 1,2,4-trichlorobenzene[57], nitrobenzene[57], etc. at a concentration of the starting materials in the range 0.6–5.0 M in the temperature range 180–220°C for several hours and in many cases also at higher temperatures (see below).

It is noteworthy that, whereas in the polycondensation of phenolphthalein and aromatic dicarboxylic acid chlorides in ditolylmethane the polyarylate precipitates from the reaction medium during its formation in the form of a thick sparingly soluble mass, in the synthesis of polyarylates in a medium which dissolves the polymer unfolded rigid macromolecular conformations are produced preferentially which results in the formation of fibrous structures, while the polymer synthesised in ditolylmethane is made up of not altogether regular globular ~ 1000 Å particles, which in turn consist of still smaller also nearly spherical 30–40 Å particles[57].

Thus in the synthesis of polymers with rigid macromolecular chains, it is necessary to make a correct choice of the reaction medium bearing in mind its influence on the selection of particular macromolecular conformations during the synthesis.

In the synthesis of crystallisable cardopolyarylates[59,60], particularly the polyarylate produced from 9,9-bis-(*p*-hydroxyphenyl)-10-anthrone and terephthalic acid, the process conditions affect not only the molecular weight but also the structure of the polymer. It is most crystalline when the polycondensation is carried out at 220°C in Sovol, 1,2,4-trichlorobenzene, and similar solvents; the polymer is obtained in amorphous form on rapid heating of a 0.6 M solution of the starting materials in Sovol at 330°C, the solution being kept at this temperature for 1 h with subsequent rapid cooling of the reaction mass to room temperature[60].

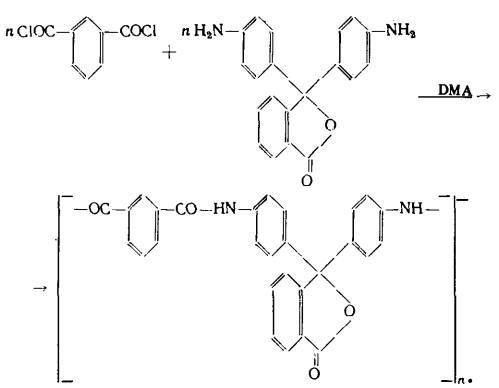
High-molecular-weight thermoreactive mixed polyarylates based on phenolphthalein, aromatic dicarboxylic acid chlorides, trihydric alcohols (for example trishydroxymethylpropane), the chlorides of unsaturated dicarboxylic

acids, for example fumaric acid, or 2,2-di-(3-allyl-4-hydroxyphenyl)propane[61,62] have been synthesised.

2. Aromatic Polyamides

The low basicity of aromatic diamines, including cardodiamines, and the high softening temperatures of cardopolyamides rule out the possibility of their successful formation by polycondensation in the melt. The method of interfacial polycondensation is also relatively unsuitable owing to the low solubility of cardodiamines and even their hydrochlorides in water. Cardopolyamides have been obtained by interfacial polycondensation only on the basis of 3,3-bis-(*p*-carboxyphenyl)phthalide and aliphatic diamines[63,64].

Cardopolyamides are usually synthesised by the low-temperature polycondensation of dicarboxylic acid chlorides and primary diamines in aprotic dipolar solvents, for example *NN*-dimethylacetamide (DMA) and *N*-methylpyrrolidinone (NMP) which function both as solvents for the starting materials and the polymers and as acceptors for the hydrogen chloride liberated[63-67], for example:



Polymers with the highest molecular weight are obtained by adding the solid acid chloride to a solution of the diamine between −10° and −30°C and stirring the reaction mixture at this temperature for 15–60 min. Although the high solubility of cardoamides makes it unnecessary to introduce into the reaction medium inorganic salts (LiCl), which are often used in the synthesis of other aromatic polyamides and when they are extruded as fibres from solutions.

3. Polyimides

Cardopolypyromellitimides obtained from anilinephthalein [3,3-bis-(*p*-aminophenyl)phthalide] and its imide were the first soluble examples of these extremely heat-resistant polymers[68,69]. Like other polyimides, they are synthesised by two-stage polycondensation with thermal cyclodehydration of the high-molecular-weight polyaminoacid obtained beforehand[68,69]. In the synthesis of cardopolyimides, it was shown that the heat treatment of polyaminoacids entails, together with intramolecular cyclisation, also solid-phase polycyclisation involving the terminal anhydride and amino-groups, leading to an increase of the molecular weight of the polyimide[70].

Single-stage high-temperature polycyclisation in an organic solvent (nitrobenzene, benzonitrile, α-chloronaphthalene, sulpholane, cresol, etc.) has been used successfully to synthesise high-molecular-weight soluble cardopolyimides[71-74]. The difference of this method from the two-stage version is that in the single-stage polycyclisation the growth of the polymer chain (the polymerisation reaction proper) takes place simultaneously with ring closure. This has been demonstrated both by kinetic studies (the rate of reaction is limited by the formation of the amidoacid and not by its cyclodehydration[75,76]) and by the discovery that the molecular weight of the polyimide increases slowly and gradually with duration of the reaction[73,74]. It has been shown for the reaction of anilinephthalein with pyromellitic anhydride and also of anilinephthalein and 9,9-bis-(*p*-aminophenyl)fluorene with the dianhydride of di-(3,4-dicarboxyphenyl) ether in nitrobenzene at 180°C that the rate of reaction is more sensitive to the change in the nature of the tetracarboxylic acid dianhydride than in the diamine[75,76].

It is noteworthy that single-stage high-temperature polycyclisation is applicable also to the synthesis of other high-molecular-weight soluble or insoluble and fusible or infusible polyimides[77,78].

The formation of polyimides from tetracarboxylic dianhydrides and primary diamines is a reversible reaction[72,73,76]. Therefore, in order to obtain high-molecular-weight polyimides, it is necessary to remove from the reaction medium as far as possible the water formed on cyclisation, which is achieved in high-temperature cyclisation by raising the reaction temperature and by carrying out the process in a stream of an inert gas, by binding the water with chemical agents (acid anhydrides and chlorides, carbodi-imides, etc.), and by employing a vacuum in the two-stage process.

High-molecular-weight cardopolyimides are also obtained by the cyclisation in solution of high-molecular-weight polyamidoacids in the presence of a mixture of carboxylic acid anhydrides and tertiary amines at 20–100°C without the intermediate formation of the final moulded objects from the polyamidoacids[79].

Cardopolyimides have also been successfully synthesised[80,81] by two-stage polycyclisation of the dichlorides of tetracarboxylic acid diesters and primary diamines. Cyclisation of the intermediates (polyamidoesters) which are much more resistant to hydrolysis than polyamidoacids, leads to the formation of carbopolyimides with higher molecular weight than those obtained by the cyclodehydration of the corresponding polyamidoacids, best results being obtained by the cyclisation of polyamidoesters in nitrobenzene at 210°C or by treatment in solution in amide-type solvents with a mixture of acetic anhydride and pyridine. The cyclisation of polyamidoesters is also a reversible process[80] since polyimides readily undergo methanolysis.

The study of the kinetics of the solid-phase polycyclisation of cardopolyamidoesters in films showed that the process follows first-order kinetics in the initial stage, the rate of cyclisation increasing with the basicity of the diamine used to prepare the polyamidoester ($k_c = 7.10 \times 10^{-2}$ and 3.10×10^{-2} min^{-1} at 200°C for the polypyromellitamidoesters derived from 9,9-bis-(*p*-aminophenyl)fluorene and anilinephthalein respectively[82]).

4. Poly-1,3,4-oxadiazoles

Cardopoly-1,3,4-oxadiazoles have been synthesised using 3,3-bis-(*p*-carboxyphenyl)phthalide and its derivatives (the dichloride and the dihydrazide) as the starting materials[83-86]. Two methods were chosen for its synthesis and investigated: a two-stage method designed to

prepare high-molecular-weight polyhydrazides with subsequent cyclodehydration and single-stage polycyclisation in polyphosphoric acid (PPA).

The characteristics of the low-temperature polycondensation of the dihydrazide and the dichloride of 3,3-bis-(*p*-carboxyphenyl)phthalide and also of either of these compounds coupled with the corresponding derivatives of other dicarboxylic acids are similar to those of the formation of other polyhydrazides with the sole difference that the high solubility of cardopolyhydrazides makes it possible to carry out the reaction not only in hexamethylphosphoramide but also in solvents such as NMP and DMA. It is also noteworthy that in the synthesis of mixed polyhydrazides the reaction takes place more successfully when one of the initial dihydrazides is that of 3,3-bis-(*p*-carboxyphenyl)phthalide coupled with the chloride of another acid. This is probably due to the higher solubility of the dihydrazide compared with the dihydrazides of many other aromatic dicarboxylic acids, the higher rate of the main process, and the consequent decrease of the contribution by side reactions.

Apart from the thermal cyclisation of polyhydrazides, which requires extremely high temperatures, the chemical cyclisation method for the conversion of cardopolyhydrazides into poly-1,3,4-oxadiazoles has become possible and has proved extremely effective. It consists in the treatment of the polyhydrazide in solution at 100°C for 5 h with the dimethylformamide (DMF)–sulphur trioxide complex[86]. The resulting polymer is identical in structure to the poly-1,3,4-oxadiazole obtained by the thermal cyclodehydration of the polyhydrazide at 300°C for 35 h in a vacuum of 10^{-3} mmHg.

A particularly successful method of synthesising solid cardopoly-1,3,4-oxadiazoles is single-stage polycyclisation in PPA at 140–150°C for 5 h.[86] An unusual feature of the synthesis of cardopoly-1,3,4-oxadiazoles in PPA consists in the fact that soluble linear polymers are formed only when equimolar amounts of 3,3-bis-(*p*-carboxyphenyl)phthalide and its dihydrazide interact. This is because in the reactions according to other generally adopted schemes, based on the acid and hydrazinium sulphate or the acid dihydrazide alone, there are side reactions between the lactone ring and hydrazine or the dihydrazide[86]. The molecular weight of the polymer depends on the concentration of phosphorus pentoxide in PPA, increasing markedly with the latter, starting from about 82%.

The study of the formation of poly-1,3,4-oxadiazoles also shows that the method of synthesis affects the structure of the polymer[87]. Thus, in contrast to the insoluble crystalline poly(1,3,4-oxadiazole-2,5-diyl-1,4-phenyleneoxy-1,4-phenylene) obtained by the thermal cyclisation of the corresponding polyhydrazide, in the single-stage polycyclisation in PPA the product is an amorphous polymer soluble in a *sym*-tetrachloroethane–phenol mixture (3 : 1, w/w).[87]

5. Other Polymers

Aromatic cardopolyethers derived from phenolphthalein, obtained by the nucleophilic substitution of activated aromatic dihalogeno-compounds and alkali metal bisphenoxides in dimethyl sulphoxide (DMSO)[36], were already mentioned above. The formation of polyethers from cardobisphenols (phenolphthalein, 9,9-bis-(*p*-hydroxyphenyl)fluorene proceeds less vigorously than the reaction with bisphenols such as 2,2-di-(*p*-hydroxyphenyl)propane, which may be due both to the reduced reactivity of the former owing to the high acidity of cardobisphenols and to the heterogeneity of the reaction medium owing to the low solubility of such alkali metal bisphenoxides. High-molecular-weight polyethers based on cardobisphenols have been obtained using as the initial dihalogeno-compound di-(*p*-fluorophenyl) sulphone and 4,4′-difluorobenzophenone, which are more reactive than their chlorinated analogues, and at higher temperatures (170–185°C) than other polyethers[36].

Despite the opening of the lactone ring of phenolphthalein in alkaline media (see above), aromatic polyethers based on it are soluble, have high molecular weights, and their lactone rings remain unaffected, which rules out the possibility of reaction between the dihalogeno-compound and the carboxy anion of the open-chain form of phenolphthalein [(B) and (C), see p.552]. Owing to the reactivity of the NH-group of the lactim ring of 3,3-bis-(*p*-hydroxyphenyl)phthalimidine in the formation of the polyester from it and di-(4-fluorophenyl) sulphone, the NH group is also involved in the reaction, which results in the formation of an insoluble and probably structured polymer.

The preparation of soluble and fusible aromatic homo- and mixed cardopolyanhydrides from 3,3-bis-(*p*-carboxyphenyl)phthalide by low-temperature polycondensation in solution has been described[88]. The chloride of 3,3-bis-(*p*-carboxyphenyl)phthalide or a mixture of this chloride with 3,3-bis-(*p*-carboxyphenyl)phthalide are employed for the synthesis of homopolyanhydrides. In the first case, the polycondensation is achieved in the presence of water.

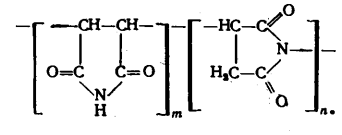
Cardobisphenols [phenolphthalein, fluoroscein, *o*-cresolphthalein, 1,1-bis-(*p*-hydroxyphenyl)cyclohexane, etc.] have been used successfully to synthesise thermoreactive polymers of the phenol-formaldehyde type[89–92]. Owing to the insolubility of such bisphenols in water, the polymers were formed in solvents such as DMF and n-propyl alcohol[89] in the presence of aqueous ammonia as a catalyst. The polymers become infusible and insoluble on heating at 160–180°C.

Many high-molecular-weight (with M_W up to 100 000 and above) carbon chain cardopolymers have also been synthesised: polymethylenephthalide, polymethylenephthalimidine, polyacenaphthene, etc.[92–98] They are synthesised by the usual polymerisation methods: the high melting point of the monomers hinders polymerisation in bulk, since such polymerisation requires the initial fusion of the monomer.

It has been shown that the resistance of methylenephthalimidines to polymerisation is lower than that of methylenephthalide, which is probably due to the greater steric hindrance in the former monomer.

An unusual monomer of the cardo-type is maleic anhydride the capacity of which for homopolymerisation was clearly demonstrated as late as 1961–1963.[99–103] It was established that maleic anhydride polymerises via a radical mechanism under the influence of γ-radiation or in the presence of a high sensitiser concentration (for example 5% benzoyl peroxide).

Maleimide, the nitrogen analogue of maleic anhydride, polymerises via radical and ionic mechanisms[104,105], the ionic polymerisation proceeding partly with migration of hydrogen atoms and the formation of a polymer with the following structure[105]:



III. PROPERTIES

We shall consider initially the effect of the chemical structure of the polymer on its heat resistance and solubility. The joint examination of such seemingly different properties is not fortuitous, since the effect of cardo-groups has the greatest influence precisely on these polymer characteristics.

One of the ways of obtaining heat resistant polymers is the synthesis of rigid-chain macromolecules with large segments, which leads to high glass temperatures. In many cases the glass temperature of rigid-chain polymers may be above the temperature of the onset of their vigorous decomposition and the latter then determines the temperature range in which the polymer may be used.

Thus there is a serious contradiction between the attempt to create the most heat resistant polymer and the possibility of moulding it into finished articles: the higher the heat resistance of the polymer the more difficult it is to mould its melt by the usual methods. One of the ways of overcoming this difficulty involves the formation of articles from highly heat-resistant polymers in solution, which requires the creation of polymers combining a high rigidity of its component macromolecules and a high solubility†.

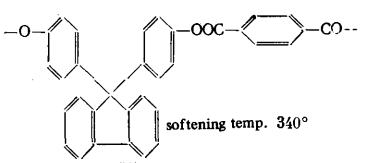
The introduction of various rings into the main macromolecular chain, the enhancement of the intermolecular interaction owing to polar groups and hydrogen bonds, the introduction of cyclic side groups, the crystallisation of the polymer, an increase in the degree of order in the supermolecular structure, the employment of starting compounds with a symmetrical structure (for example the replacement of isophthalic acid by terephthalic acid), the formation of chemical cross-links between linear macromolecules, a regular distribution of chain units, conversion into stereoregular polymers, etc. lead to an increase of the heat resistance of linear polymers.

Solubility is improved mainly by the conversion of the polymer into an amorphous form, an increase of the rigidity of the macromolecular chain, the introduction of polar groups with an affinity for the solvent (i.e. leading to a positive heat of mixing), the introduction of various substituents "loosening" the polymer structure, the introduction of cyclic side groups containing polar groups with an affinity for the solvent, the breakdown in the order of alternation of chain units and the introduction of units of different kinds, etc. In many cases one of these factors is insufficient for a significant improvement of the solubility—a combination of various factors is necessary.

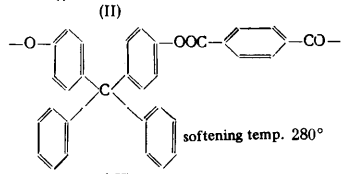
Comparison of the factors leading to an improvement of heat resistance and of solubility shows that some of these improve one property and impair the other (for example a decrease of rigidity improves solubility but lowers heat resistance, etc.) It would be most interesting to achieve a simultaneous increase of the heat resistance of polymers and of their solubility. This can be done by introducing cyclic side groups into the macromolecule. An appreciable effect is obtained when cardo-groups are introduced.

† Therefore infusible and insoluble, as a rule heterocyclic, polymers are moulded mainly at an intermediate stage of their synthesis—the soluble pre-polymers (polyamidoacids, polyhydrazides, etc.)—which has its disadvantages relating to the removal of water and the solvent, which impairs the integrity of the finished article, and a number of other unfavourable complications[72,106].

The superior heat resistance of the polyterephthalate of 9,9-bis-(*p*-hydroxyphenyl)fluorene (II) compared with the polyterephthalate of 4,4′-dihydroxytetraphenylmethane (III) is instructive in this sense:



(II)



(III)

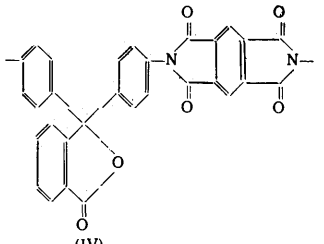
As already stated, one of the ways of increasing heat resistance is crystallisation of the polymer. Since many cardopolymers have an amorphous structure, it has come to be believed that the increase of the rigidity of the polymer chain as a result of the introduction of cardo-groups and crystallisation are largely mutually exclusive factors, since crystallisation requires the presence of chains with a symmetrical structure and a powerful interaction between the chains, while bulky substituents, such as cardo-groups in particular, hinder it[106]. That this is a mistaken view was demonstrated subsequently by the synthesis of crystallisable polyarylates derived from 9,9-bis-(*p*-hydroxyphenyl)-10-anthrone, the structure of which may be varied both by the conditions of synthesis and by the conditions in the subsequent treatment of the polymer[59,60]. Other cardopolymers in different structural forms can also be obtained, for example polyarylates derived from 9,9-bis-(*p*-hydroxyphenyl)fluorene and 1,1-bis-(*p*-hydroxyphenyl)-cyclohexane[107]. These factors, in conjunction with the finding that polyarylates from phenolphthalein as well as other cardopolyheteroarylenes containing phthalide groups are amorphous non-crystallisable polymers lead to the hypothesis, based on the asymmetric structure of the phthalide group, that the structure of such polymers resembles that of atactic polymers. Like atactic polymers, cardopolymers with phthalide groups in the chain contain an asymmetric substituent distributed at random.

Presumably under certain conditions it is possible to achieve a stereoregular distribution of the phthalide groups and the formation of a crystalline polymer is then possible.

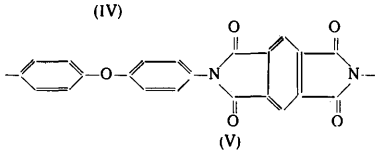
The crystallinity of cardopolymers and others must be taken into account when their properties are compared, since it affects[107] the heat resistance and the thermal stability of the polymers, their solubility, etc. Therefore, in order to compare polymers with different chemical structures, it is best to employ data for amorphous polymers.

As already stated, cardo-groups increase the rigidity of the main chain and loosen the polymer, which improves the solubility. The solubilisation of rigid-chain polymers such as polypyromellitimides due to cardo-groups appears particularly striking. Thus the polypyromellitimide derived from anilinephthalein (IV), which has a glass temperature of 485°C, is readily soluble in DMF, DMA, nitrobenzene, *sym*-tetrachloroethane, cresol, hexafluoroacetone sesquihydrate, etc., in contrast to the familiar

polyoxydiphenylenepyromellitimide (V), which is insoluble in known organic solvents:

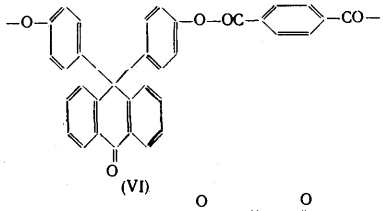


(IV)

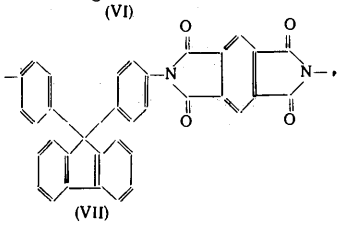


(V)

The solubility of cardopolymers with polar groups is much higher than that of polymers with less polar cardo-groups while their heat resistance is approximately the same. Thus the 9,9-bis-(*p*-hydroxyphenyl)-10-anthrone polyarylate (VI) are more soluble than the 9,9-bis-(*p*-hydroxyphenyl)-fluorene polyarylate (II) despite their higher tendency towards crystallisation while the polypyromellitimide derived 9,9-bis-(*p*-aminophenyl)fluorene (VII) does not dissolve in any of the known organic solvents in contrast to the polyimide (IV):



(VI)



(VII)

1. Polycarbonates

The properties of cardopolycarbonates derived from bisphenols and based on 2-norbornanone and analogous ketones, cyclohexanone, etc. have been investigated in greatest detail[108-114]. Such polycarbonates have an amorphous structure and dissolve in chlorinated and saturated aliphatic hydrocarbons: CH_2Cl_2, $CHCl_3$, 1,2-dichloroethane, aromatic hydrocarbons (benzene and toluene), cyclohexanone, and dioxan; they swell in aliphatic ketones. Their enhanced solubility is probably associated with the large size of the non-planar cardo-group, which leads to an appreciable loosening of the polymer. At the same time, the presence of cardo-groups leads to an increase of the heat resistance of the polymers and it is interesting that the glass temperature increases with the dimensions of the cardo-group of the norbornane type. The high glass temperatures of such polycarbonates are due to the fact that the non-coplanar groups of the norbornane type, which are very bulky in various directions, cannot be oriented in any particular direction and therefore cannot "migrate" in the small space between the molecular chains to the same extent as, for example, alkyl or phenyl groups[108].

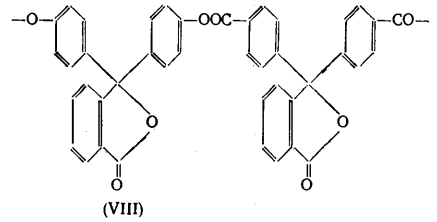
Polycarbonates derived from phenolphthalein and its derivatives show an even higher heat resistance while retaining a high solubility. The somewhat greater range of solvents for the polycarbonate from phenolphthalein compared with the polycarbonate from 3,3-bis-(*p*-hydroxyphenyl)phthalimidine is striking; this is probably due to intermolecular hydrogen bonds in the second polymer. At the same time it dissolves in chloroform, while the corresponding polyterephthalate is insoluble in chlorinated solvents owing to hydrogen bonding[115].

2. Polyarylates

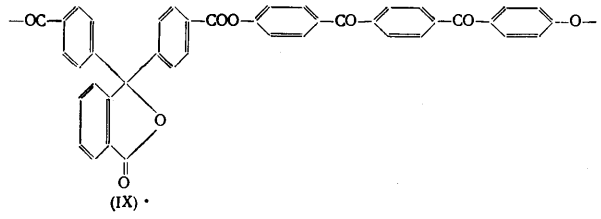
As already stated, the characteristics of cardopolymers were discovered for the first time for polyarylates; it is therefore natural that their properties have been investigated in greatest detail, which in turn required the synthesis of a wide variety of examples of this class of polymers differing in the nature of the cardo-group and other moieties of the macromolecule. They include polyarylates derived from phenolphthalein[19,20,34,54,116-127], 4,5,6,7-tetrachlorophenolphthalein[128], 3,3-bis-(*p*-hydroxyphenyl)phthalimidine[34,129-131], 3,3-bis-(*p*-hydroxyphenyl)-2-phenylphthalimidine[37,52,53,132], 2-ethyl-3,3-bis-(*p*-hydroxyphenyl)-phthalimidine[133], 2-(β-chloroethyl)-3,3-bis-(*p*-hydroxyphenyl)phthalimidine[134], phenolsulphophthalein[135], 9,9-bis-(*p*-hydroxyphenyl)fluorene[113,136-139], 9,9-bis-(*p*-hydroxyphenyl)-10-anthrone[59,95,113,114,132], and many other cardobisphenols and dicarboxylic acids[56,140-149].

The main characteristic feature of these polymers is heat resistance, greatly exceeding the heat resistance of polyarylates which have a similar structure but do not contain cardo-groups. The polyarylates devised from 9,9-bis-(*p*-hydroxyphenyl)fluorene and 4,4'-dihydroxytetraphenylmethane were already compared above in this sense.

Another clear example is provided by the much higher heat resistance of polyarylate (VIII) (softening temperature 340°C)[150] compared with the isomeric polyarylate (IX) (270°C)[142]:



(VIII)

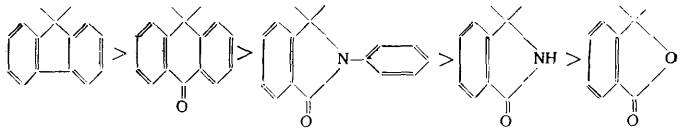


(IX)

The influence of the cardo-group on the softening temperature is shown particularly clearly in polyarylates synthesised from aliphatic dicarboxylic acids. Thus the softening temperatures of polyarylates from phenolphthalein

and 2,2-di-(*p*-hydroxyphenyl)propane on the one hand and sebacic acid on the other are 100° and 36°C respectively.

Estimation of the "intrinsic" contribution of various cardo-groups to a heat resistance of polyarylates showed that they can be arranged in the following series in terms of the decrease of their contribution[114]:



K_i/M 1.58 1.56 1.55 1.43 1.40

where K_i/M is the ratio of the "reduced" volume of the ring to its molecular weight[151]. Above it was stated that, depending on the nature of the solvent in which the polyarylates are synthesised, coiled or uncoiled conformations are produced, which entails the formation of globular (synthesis in a non-solvent medium) or fibrous (synthesis in a medium dissolving the polymer) forms of supermolecular structures respectively[50,51,57,152]. The supermolecular structure of polyarylates has a significant influence on the entire set of their physical properties. Table 1 shows that, for identical molecular weights, the specific impact strength of a polyarylate synthesised in "good" solvents (Sovol, α-chloronaphthalene, nitrobenzene) is higher by a factor of 4–10 than that of the same polyarylate synthesised in ditolylmethane. The elongation on rupture also increases severalfold.

Table 1. Properties of the polyarylates synthesised from phenolphthalein and isophthalic acid by high-temperature polycondensation in various media[51].

Property	Medium used in synthesis				
	ditolylmethane	Sovol	α-chloronaphthalene		nitrobenzene
Structure	globular	← fibrous →			
Molecular weight M_w	28000	33000	28000	48000	26000
Softening temperature, °C*	270	280	290	300	275
Tensile strength (film), kgf cm^{-2}	640	640	740	780	650
Elongation on rupture (film), %	10—20	85	80	100	40—70
Specific impact strength (monolithic specimen), kgf cm^{-2}	2—3	11	10	20	14

* The temperature at which the strain in the monolithic specimen relaxes to zero was adopted[150].

The more satisfactory physicomechanical parameters of the fibrous polyarylate obtained from 3,3-bis-(*p*-hydroxyphenyl)-2-phenylphthalimidine by high-temperature polycondensation in a medium dissolving the polymer compared with the corresponding polyarylate having a globular supermolecular structure and obtained by interfacial polycondensation (Table 2) suggests that high-temperature polycondensation is perhaps a more successful method of synthesising polyarylates[51].

Although the majority of cardopolyarylates are amorphous, many of them have a distinct tendency to become ordered. Among the latter, the polyarylate obtained from 9,9-bis-(*p*-hydroxyphenyl)-10-anthrone and terephthalic acid, which can be synthesised with a high degree of crystallinity[60], is outstanding. The structure and hence the properties of this polymer can be regulated both by varying the conditions of synthesis and by appropriate treatment of the finished polymer. The polymer is obtained in the most crystalline form on polycondensation at 220°C in solvents such as Sovol, 1,2,4-trichlorobenzene, nitrobenzene, and α-chloronaphthalene.

Table 2. Properties of the polyarylates synthesised from 3,3-bis-(*p*-hydroxyphenyl)-2-phenylphthalimidine and terephthalic acid[51].

Property	Method of synthesis	
	interfacial	high-temperature, in solution
Softening temperature, °C	280–285	315–320
Tensile strength (film), kgf cm^{-2}	960	1000
Elongation on rupture (film), %	13	40–50
Specific impact strength (monolithic specimen), kgf cm^{-2}	1	7–9

By successive treatment of such a polymer by various solvents, it is possible to crystallise the amorphous polyarylate and conversely to obtain the amorphous polymer from a crystalline specimen. For example, when amorphous polyarylate is treated with chloroform in a swollen state, it crystallises, while reprecipitation of crystalline polyarylate with the same chemical structure from solution in a 3 : 1 (by weight) tetrachloroethane (TCE)–phenol mixture results in the formation of an amorphous polymer[107]. The crystalline polyarylate does not soften up to the onset of its decomposition and dissolves only in a 3 : 1 (by weight) tetrachloroethane–phenol mixture, while in the amorphous form it softens at 325–365°C and dissolves readily in various organic solvents[107,118]. Polyarylates obtained from 9,9-bis-(*p*-hydroxyphenyl)fluorene also show a tendency to crystallise, albeit to a smaller extent[107,118].

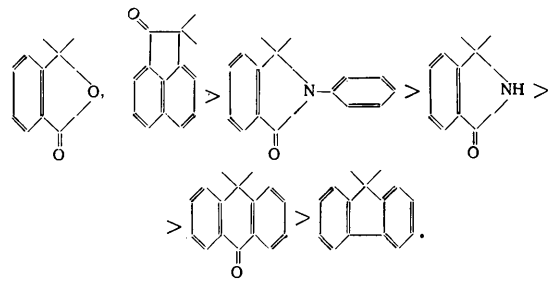
The crystallisability of cardopolyarylates depends not only on the nature of the cardo-group but also on the component in which it is introduced into the macromolecule. Thus the polyarylate obtained from hydroquinone and 9,9-bis-(*p*-carboxyphenyl)-10-anthrone, which is isomeric with the polyarylate 9,9-bis-(*p*-hydroxyphenyl)-10-anthrone and terephthalic acid, has an amorphous structure, in contrast to the latter[132]. Cardopolyarylates derived from phenolphthalein have a certain degree of order only when an acid with a cardo-group in the molecule is employed as the initial component[119], for example polyarylate (VIII), which may be due to the fact that, while the phthalide group itself is asymmetric, the macromolecule as a whole becomes more symmetrical.

Certain cardopolyarylates derived from 3,3-bis-(*p*-hydroxyphenyl)phthalimidine and 2-(β-hydroxyethyl)-3,3-bis-(*p*-hydroxyphenyl)phthalimidine also show some tendency towards becoming ordered, which may be consequence of hydrogen bonds influencing also the solubility of such polymers[129–131].

The presence in the polymer chain of cardo-groups results in a high solubility of such polyarylates in many organic solvents. Polyarylates from phenolphthalein and aromatic dicarboxylic acids are soluble in methylene chloride, chloroform, 1,2-dichloroethane, *sym*-tetrachloroethane, tetrahydrofuran (THF), cyclohexanone, DMF, and others with formation of highly concentrated solutions

(> 25%).[19,20] The increase of solubility as a result of the introduction of cardo-groups (for example the phthalide group) is also achieved when they are present at a very low concentration in the macromolecules of copolymers. For example, the mixed polyarylate obtained from terephthalic acid, phenolphthalein, and 2,2-di-(*p*-hydroxyphenyl)propane (in molar proportions of 1.0 : 0.15 : 0.85) is readily soluble in chloroform[20]. An analogous enhancement of solubility is achieved by the introduction of the phthalide group into the polymer chain as part of the acid component[56,119].

Comparison of the contributions of various cardo-groups to the increase of the solubility of polyarylates suggests that they can be arranged in the following sequence:



The highest solubility of polymers with phthalide and phthalimidine groups is probably due to the greater dimensions, polarity, and asymmetry of the structure of such groups. The somewhat lower solubility of polyarylates containing fluorene and anthrone cardo-groups is probably due to their greater symmetry, which leads to the crystallisation of such polymers.

The solubility of polymers containing phthalimidine cardo-groups is due to the presence or absence of mobile hydrogen atoms. Thus polyarylates from 3,3-bis-(*p*-hydroxyphenyl)phthalimidine or 2-(β-hydroxyethyl)-3,3-bis-(*p*-hydroxyphenyl)phthalimidine dissolve only in solvents which rupture intermolecular hydrogen bonds[39,129-131], while polyarylates from 3,3-bis-(*p*-hydroxyphenyl)-2-phenylphthalimidine in which the mobile hydrogen atom is replaced by the phenyl group, dissolve even in chloroform and methylene chloride[38,52,53].

The solubility of cardopolyarylates makes it possible to determine their molecular weight and to establish the relation between the intrinsic viscosity of their solutions and the molecular weight (Table 3). The properties of solutions of cardopolyarylates have been described in dissertations and in a monograph[152-155]. The method of synthesis affects not only the physicochemical properties of polyarylates but also their molecular-weight characteristics (Table 3).

The study of thermal and thermo-oxidative degradation of polyarylates showed[162-172] that, according to dynamic thermogravimetric (TG) data (in an atmosphere of helium at a heating rate of 5 deg min^{-1}), the onset of the decrease of the weight of various polyterephthalates occurs at 350–360°C and their vigorous decomposition takes place at 460–470°C.[172] The polyarylate obtained from terephthalic acid and 9,9-bis-(*p*-hydroxyphenyl)fluorene begins to decompose at a temperature higher by 10–15 deg than the other polymers. Cardopolyarylates differ from one another mainly in the amount of carbon residue at 900°C. Polyarylates from 9,9-bis-(*p*-hydroxyphenyl)-10-anthrone, 9,9-bis-(*p*-hydroxyphenyl)fluorene, and 2,2-bis-(*p*-hydroxyphenyl)-1-acenaphthenone, in which there are two aromatic rings in the cardo-group, decompose in an inert atmosphere to the extent of 43–44% regardless of the presence of absence of a carbonyl group, while the polyterephthalate synthesised from phenolphthalein loses 50% of its weight.

Table 3. The values of the parameters K and a in the Mark–Houwink equation for cardopolyarylates.

Polymer	Method of synthesis	Solvent for determination of $[\eta]^{20°}$	$K \times 10^4$	a	References
Polyarylate from phenolphthalein and isophthalic acid	High-temperature polycondensation in ditolylmethane	*sym*-Tetrachloroethane	16.4	0.53	152,156
		Tetrahydrofuran	52.3	0.39	152,156
Ditto	Interfacial polycondensation	*sym*-Tetrachloroethane	3.35	0.67	152,156
		Tetrahydrofuran	21.3	0.46	152,156
Polyarylate from phenolphthalein and terephthalic acid	High-temperature polycondensation in ditolylmethane	*sym*-Tetrachloroethane	2.42	0.696	156
		Tetrahydrofuran	6.357	0.596	156
		Dioxan	10.30	0.549	156
Ditto	High-temperature polycondensation in Sovol	*sym*-Tetrachloroethane	6.36	0.596	156
Ditto	Acceptor-catalytic polycondensation in dichloroethane	*sym*-Tetrachloroethane	5.09	0.69	157
Ditto	Acceptor-catalytic polycondensation in acetone	*sym*-Tetrachloroethane	4.42	0.73	157
Ditto	Interfacial polycondensation	*sym*-Tetrachloroethane	0.266	0.938	152-154
		Tetrahydrofuran	0.724	0.828	152-154
		Dioxan	0.883	0.800	152-154
Polyarylate from 3,3-bis-(*p*-hydroxyphenyl)-2-phenylphthalimidine and terephthalic acid	High-temperature polycondensation in Sovol	*sym*-Tetrachloroethane	6.7	0.59	158
		Tetrahydrofuran	25.85	0.488	158
Ditto	Interfacial polycondensation	*sym*-Tetrachloroethane	1.114	0.84	158
		Dioxan	3.64	0.706	
Polyarylate from 3,3-bis(*p*-hydroxyphenyl)-2-phenylphthalimidine and isophthalic acid	High-temperature polycondensation in Sovol	Tetrahydrofuran	29.20	0.415	159
Ditto	Interfacial polycondensation	*sym*-Tetrachloroethane	6.820	0.615	159
Polyarylate from 9,9-bis-(*p*-hydroxyphenyl)-fluorene and isophthalic acid	High-temperature polycondensation in ditolylmethane	*sym*-Tetrachloroethane	23.05	0.495	160,161
		Tetrahydrofuran	50.24	0.407	
Ditto	Interfacial polycondensation	*sym*-Tetrachloroethane	5.22	0.640	160,161

The study of the ageing processes of polyarylates for low degrees of conversion (250–350°C) showed that structure-formation processes predominate on heat treatment alone and on thermo-oxidation[166,168,170]. Degradation of the polymers takes place at 300–350°C together with structure formation, as shown by the splitting of the maximum on the molecular-weight distribution curve[166-168]. At higher temperatures (350–500°C), more far-reaching changes take place, accompanied by the formation of solid and gaseous low-molecular-weight products and of a solid carbonised residue[165-170].

The resistance of cardopolyarylate based on phenolphthalein and 9,9-bis-(*p*-hydroxyphenyl)fluorene to the action of ionising and ultraviolet radiation in films and solutions has been studied[121,173-176].

3. Aromatic Polyamides

Another type of cardopolymers which exhibit all the specific features are aromatic polyamides (Table 4). In contrast to many aromatic polyamides, cardopolyamides have an amorphous structure. A tendency has been noted towards the ordering of polyamides derived from 9,9-bis-(*p*-aminophenyl)fluorene and terephthalic acid (when the solution of the polymer in DMF is allowed to stand) and from 9,9-bis-(*p*-aminophenyl)fluorene and isophthalic acid (when its solution in cyclohexanone is allowed to stand). Despite their amorphous structure, the heat resistance of cardopolyamides is much higher than that of other polyamides. Thus the polyamide from 9,9-bis-(*p*-aminophenyl)fluorene and isophthalic acid softens at 385°C,[65] while the widely familiar poly-*m*-phenyleneisophthalamide has a glass temperature of 270°C. The softening temperature of the cardopolyamide is always higher than that of the corresponding cardopolyarylate[186].

Table 4. Cardopolyamides[a]

No.	Starting materials		Polymer			References
	diamine	dicarboxylic acid chloride	d, g cm^{-3}	$\eta_{ln}^{25°}$ in DMF, dl × g^{-1}	softening temp.[b], °C	
1	2	3	4	5	6	7
1	3,3-Bis-(4'-aminophenyl) phthalide	Adipic	1.213	0.57	240	65,177,178
2	Ditto	Sebacic	1.195	0.94	220	65,177,178
3	»	Fumaric	—	0.19	530 (decomp.)	65,177,178
4	»	Isophthalic	1.298	1.14	385	65,177,178
5	»	Terephthalic	1.302	1.45	390	65,177,178
6	»	Biphenyl-4,4'-dicarboxylic	1.271	0.79	395	65,177,178
7	»	Di-(*p*-carboxyphenyl) ether	1.281	1.22	340	65,177,178
8	»	3,3-Bis-(*p*-carboxyphenyl)-phthalide	1.280	0.41	385	63,64
9	»	2,2-Bis-(*p*-carboxyphenyl)-hexafluoropropane	—	0.44	390	179
10	3,3-Bis-(*p*-aminophenyl)-phthalimidine	Adipic	—	0.23	245	65,177
11	Ditto	Sebacic	1.193	0.57	225	65,177,178
12	»	Isophthalic	1.297	0.41	390	65,177,178
13	»	Terephthalic	1.297	0.74	395	65,177,178
14	»	3,3-Bis-(*p*-carboxyphenyl) phthalide	1.278	0.50	400	63, 64
15	9,9-Bis-(*p*-aminophenyl) fluorene	Isophthalic	—	1.30	350	67
16	Ditto	Terephthalic	—	1.58	405	67
17	9,9-Bis(*p*-aminophenyl)-10-anthrone	Isophthalic	—	0.75	—	
18	Ditto	Terephthalic	—	1.06	400	180
19	»	3,3-Bis-(*p*-carboxyphenyl)-phthalide	—	0.41	—	

Table 4 (continued).

No.	Starting materials		Polymer			References
	diamine	dicarboxylic acid chloride	d, g cm^{-3}	$\eta_{ln}^{25°}$ in DMF, dl × g^{-1}	softening temp.[b], °C	
1	2	3	4	5	6	7
20	1,1-Bis-(*p*-aminophenyl) cyclohexane	Terephthalic	—	1.26[c]	305	181
21	Hexamethylenediamine	3,3-Bis-(*p*-carboxyphenyl)-phthalide	—	0.26	200	63,64
22	Octamethylenediamine	Ditto	—	0.25	195	63,64
23	Piperazine	»	—	0.18	305	63,64
24	*p*-Phenylenediamine	»	1.300	0.57	380	63,64
25	Benzidine	»	1.270	0.81	385	63,64
26	Di-(*p*-aminophenyl) ether	»	1.287	0.54	320	63,64
27	Di-(*m*-aminophenyl)-sulphone	3,3-Bis-(*p*-carboxyphenyl)-phthalide	—	0.57	310	
28	Di-(*p*-aminophenyl)-sulphone	Ditto	—	0.75	365	
29	3,3-Bis-(aminomethyl)-oxacyclobutane	Adipic	—	1.04[d]	170	182,183
30	Ditto	Sebacic	—	2.82[d]	170	182,183
31	»	Terephthalic	—	1.96[d]	300	182,183
32	9,9-(Bis-(3-aminopropyl) fluorene	Ditto	—	0.97[e]	—	184
33	Di-(*p*-aminophenyl) ether	1,2-Bis-(*p*-carboxy-phenyl)carborane	—	0.50[f]	350	185
34	Bis-(*p*-aminophenyl)-ether of hydroquinone	Ditto	—	0.52[f]	350	185
35	*m*-Phenylenediamine	»	—	0.20[g]	350	185

a. All the polymers except Nos. 21 and 22 were synthesised by low-temperature polycondensation in solution and polymers Nos. 21 and 22 were obtained by interfacial polycondensation.
b. The softening temperature was determined as the point of intersection of tangents to the branches of the thermochemical curve in the region of polymer flow (heating rate 150 deg h^{-1}, pressure 0.8 kgf cm^{-2}).
c. In a DMF–5% LiCl mixture.
d. In formic acid.
e. In *m*-cresol.
f. In *N*-methylpyrrolidinone.
g. In sulphuric acid.

The activation energy for the relaxation process in polyamides is always higher than in the analogous polyarylates[178] (Table 5). This suggests that the rearrangement processes in polyamide superstructures and their elements are more difficult than in polyarylates. It has been suggested[186] that this is mainly due to the presence of hydrogen bonds between the polyamide macromolecules and to some extent also to a change in the mobility of the elements of the macromolecule caused by the replacement of the ester linkage by the amide linkage.

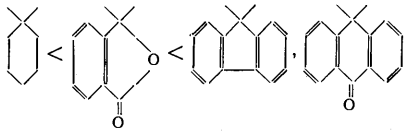
In contrast to the majority of aromatic polyamides, which are sparingly soluble in organic solvents and are mainly soluble in solutions of inorganic salts in amide

solvents, cardopolyamides are highly soluble in various amide solvents, DMSO, and cresol with formation of highly concentrated solutions (25–35%).[177] The somewhat lower solubility of polyamides with fluorene cardo-groups compared with polyamides from 9,9-bis-(*p*-aminophenyl)-10-anthrone is shown by the fact that the polyterephthalamide derived from 9,9-bis-(*p*-aminophenyl)-10-anthrone is soluble in cyclohexanone while the polyterephthalamide from 9,9-bis-(*p* -aminophenyl)fluorene does not dissolve in this solvent.

Table 5. Activation energies for the relaxation process (U_0) and molar structural constants (γ) cardopolyamides and cardopolyarylates[178].

Parameter	Polyamides from 9,9-bis-(*p*-aminophenyl) fluorene and various acids				Polyarylates from phenolphthalein and various acids	
	sebacic	isophthalic	terephthalic	diphenyl-4,4′-dicarboxylic	isophthalic	terephthalic
U_0, kcal mole^{-1}	47.5	76.3	79.5	78.9	62.7	73.0
γ, kcal mm^2 mole^{-1} kg^{-1}	1.300	0.834	1.290	1.286	1.13	1.74

A detailed study of the thermal and thermo-oxidative degradation of many cardopolyamides showed that their thermal stability depends to a high degree on the nature of the cardo-group[180,187,188], while that of polyarylates is limited mainly by the stability of the ester linkage. Cardo-groups can be arranged in the following series in terms of increasing thermal stability of polyterephthalamides[180]:



It has been shown for the highly soluble polyterephthalamides derived from anilinephthalein and 9,9-bis-(*p*-aminophenyl)fluorene[189] that branching and structure-formation processes develop at temperatures preceding the decrease in their weight (up to 350°C).

4. Aromatic Polyimides

Aromatic polyimides (Table 6) are the first examples of heterocyclic cardopolymers. The characteristics of the structure of rigid-chain cardopolymers such as polyimides affect in the first place their solubility. The only example of such polymers with the most rigid chains (polypyromellitimides), which are soluble in organic solvents while retaining their high heat resistance, are the polypyromellitimides derived from anilinephthalein and 3,3-bis-(*p*-aminophenyl)phthalimidine[68,69,72]. It is noteworthy that in the series of cardopolyimides solubility is determined not only by the chemical structure of the cardo-group but to a considerable degree also by the nature of the bridging group between the phenyl groups of the second component. Thus, in contrast to cardopolypyromellitimides, the cardopolyimides derived from biphenyl-3,3′,4,4′-tetracarboxylic acid do not dissolve in amide solvents. On the other hand, the introduction of a

Table 6. Properties of cardopolyimides.

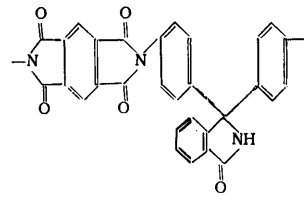
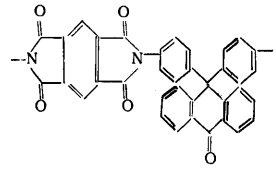
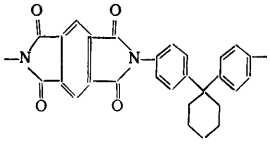
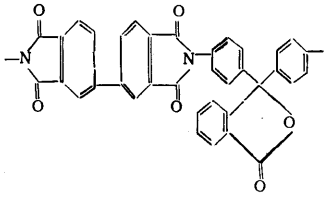
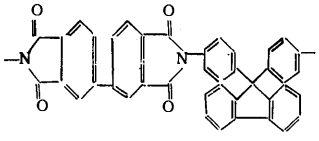
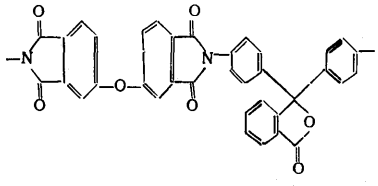
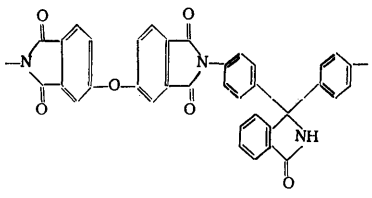
No.	Elementary unit of polyimide	η_{ln} in DMF, dl g^{-1} (25°)[a]	Density, g cm^{-3}	Softening temp., °C	References
1	2	3	4	5	6
1	IV	2.15	1.326	490[b]	68,69, 190
2		0.57	—	—	69,190
3	VII	0.65[d]	1.278	515[b]	67,69, 190
4		0.41[d]	—	—	190
5		0.35[d]	—	—	190,191
6		0.52[e]	1.325	415[c]	190
7		0.75[e]	1.260	425[b]	190
8		1.66	1.346	375[b] 360[c]	190
9		0.62	—	385[c]	190

Table 6 (contd.)

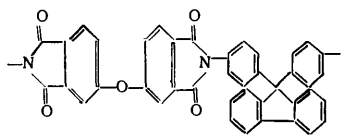
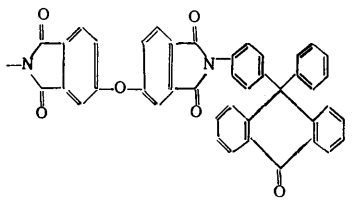
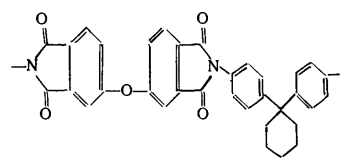
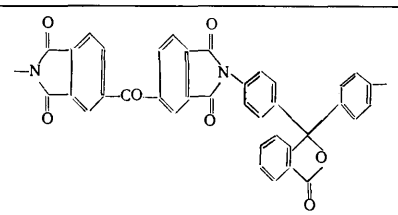
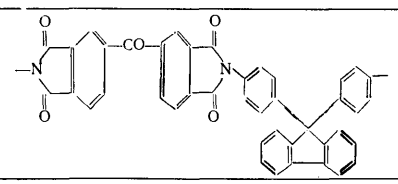
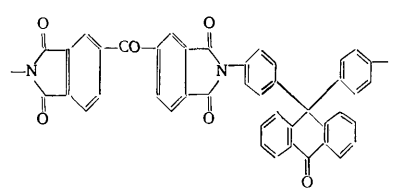
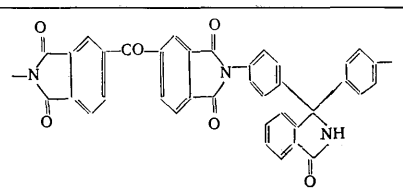
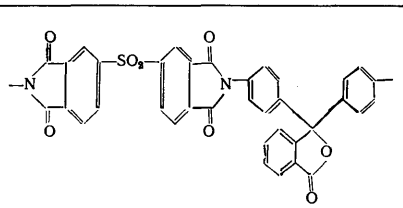
No.	Elementary unit of polyimide	$\eta_{in}^{25°a}$ in DMF, dl g^{-1}	Density g cm^{-3}	Softening temp., °C	References
1	2	3	4	5	6
10		1.20	1.280	405[b] 385[c]	190
11		1.35[c]	1.380	385[b]	190,192
12		0.33	—	285[c]	190,191
13		0.75	—	360[b] 365[c]	190
14		1.20	—	370[c]	190
15		0.64	—	370[c]	190, 192
16		0.66	—	380[c]	190
17		1.00	—	400[c]	190

Table 6 (contd.)

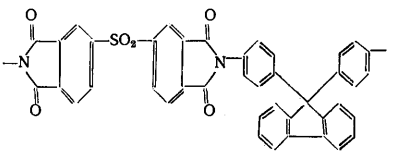
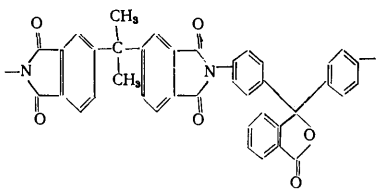
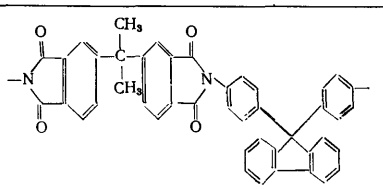
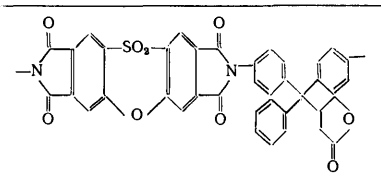
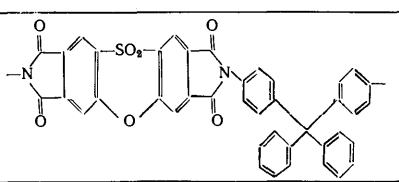
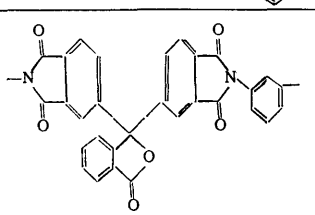
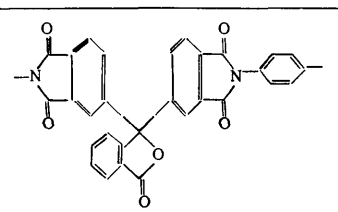
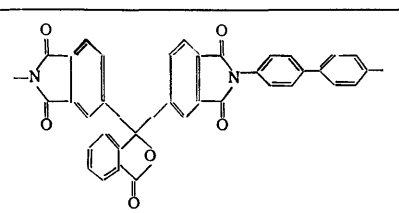
No.	Elementary unit of polyimide	$\eta_{in}^{25°a}$ in DMF, dl g^{-1}	Density, g cm^{-3}	Softening temp., °C	References
1	2	3	4	5	6
18		0.92	—	400[c]	190
19		1.01	—	355[c]	193
20		0.74	—	350[c]	193
21		1.86	—	500[c] (de-comp.)	193
22		—	—	—	193
23		0.47	—	360[c]	194
24		0.47	—	410[c]	194
25		1.17[c]	—	415[c]	194,195

Table 6 (contd.)

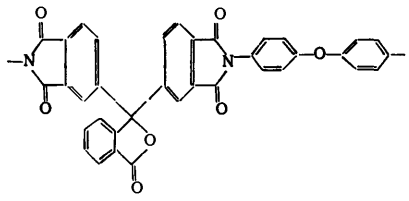
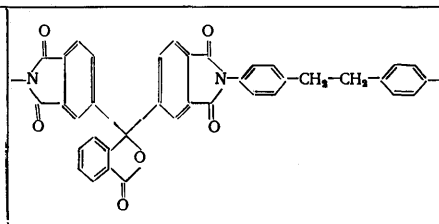
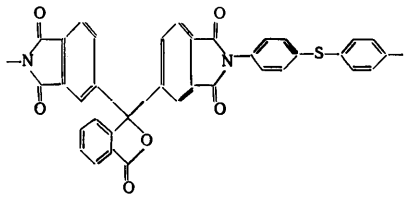
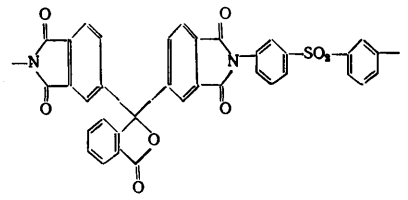
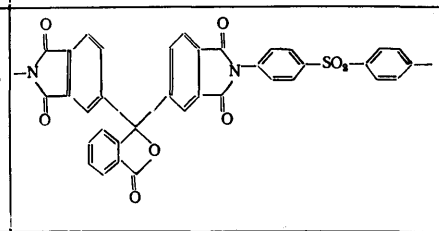
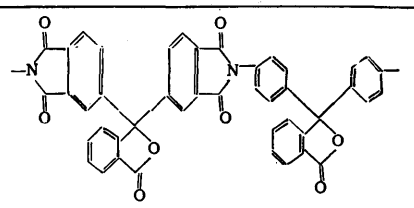
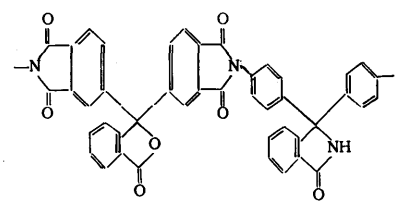
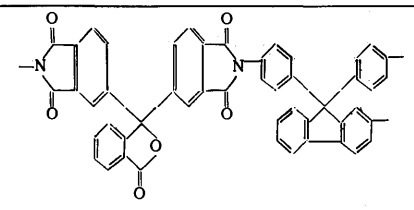
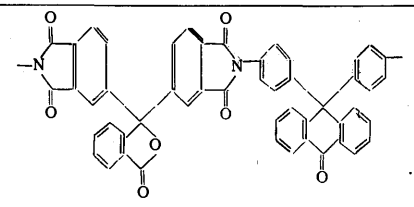
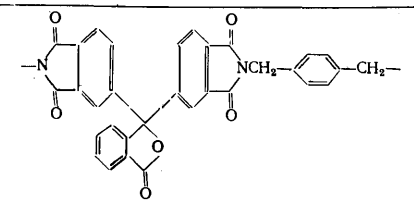
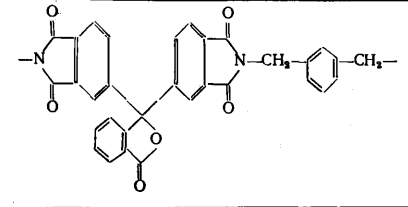
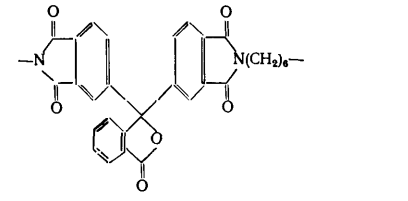
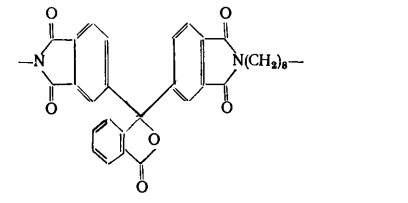
No.	Elementary unit of polyimide	$\eta_{ln}^{25°}$ a in DMF, dl g^{-1}	Density, g cm^{-3}	Softening temp., °C	References
1		3	4	5	6
26		1.36	—	345[c]	194,195
27		0.92[e]	—	315[c]	196
28		0.69	—	320[c]	194
29		0.42	—	315[c]	194
30		0.34	—	370[c]	194,19
31		1.04	—	415[c]	194,195
32		0.38	—	410[c]	194

Table 6 (contd.)

No.	Elementary unit of polyimide	$\eta_{ln}^{25°}$ a in DMF, dl g^{-1}	Density, g cm^{-3}	Softening temp., °C	References
1	2	3	4	5	6
33		1.15	—	425[c]	194
34		0.93	—	425[c]	194
35		0.37[f]	—	305[c]	78
36		0.32[f]	—	240[c]	78
37		0.86[f]	—	205[c]	78
38		0.64[f]	—	195[c]	78

a. Concentration of polymer solution 0.5 g/100 ml.
b. The softening temperature was determined in the useful operating range[150].
c. The softening temperature was assumed to be the point of intersection of tangents to the thermomechanical curve in the region of polymer flow (load 100 g, disc diameter 4 mm).
d. In sulphuric acid.
e. In *sym*-tetrachloroethane.
f. In tricresol.

carboxylic acid residue, on either group, or a carbonyl group between the phenyl rings restores the solubility of the polyimides in DMF, DMA, DMSO, and NMP and makes them soluble in methylene chloride and chloroform, while retaining their solubility in TCE.[190] An unusual feature of cardopolyimides from aliphatic diamines is that they do not dissolve in DMF but do dissolve in DMA and many chlorinated solvents[78]. The presence of two cardo-groups (phthalide or phthalide and fluorene) in the elementary unit of polyimides promotes an even greater increase of solubility, making them soluble in cyclohexanone, in which other known polyimides do not dissolve[194].

An antagonistic effect in mixtures of a number of solvents[190] has been observed for cardopolyimides obtained from di-(3,4-dicarboxyphenyl) ether, of the type which has been noted also for the polyarylate from phenolphthalein and terephthalic acid[34]. Certain cardopolyimides have a lower consolute in DMF and chloroform.

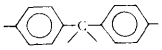
The molecular weight distribution for the polypyromellitimide obtained from anilinephthalein has been estimated and the relation between $[\eta]$ of its solution in DMF and M_w has been found[72,197,198]:

$$[\eta]^{20^\circ} = 32.83 \cdot 10^{-4}\,\bar{M}_w^{0.516}$$

together with the analogous characteristics for the polyimide from di-(3,4-dicarboxyphenyl) ether and 9,9-bis-(*p*-aminophenyl)fluorene[199]:

$$[\eta]^{20^\circ}_{DMF} = 8.91 \cdot 10^{-4}\,\bar{M}_w^{0.56},$$
$$[\eta]^{20^\circ}_{DMA} = 3.33 \cdot 10^{-4}\,\bar{M}_w^{0.65}.$$

Electron microscope and viscometric studies have shown[198] a relatively higher rigidity of the macromolecules of the polypyromellitimide obtained from anilinephthalein, which exist in solution in a coiled form. The diphenylphthalide group, where the rotation about the



linkage is hindered, is responsible for the rigid coiling of the chain[198].

Cardopolyimides can be arbitrarily divided into several groups on the basis of their heat resistance[190,200]. Polyimides from pyromellitic and naphthalenetetracarboxylic acids exhibit the highest heat resistance. An unusual feature of these polymers is that their elementary units are made up of 3–4 condensed rings. As regards this feature, they occupy an intermediate position between the usual polycondensation systems, such as aromatic polyesters and polyamides, and ladder-type polymers. As a result of this feature, these polyimides have higher softening temperatures, which are sometimes not attained owing to degradation. Monolithic specimens of cardopolyimides[200] have operating characteristics at high temperatures and stresses which are unusual for organic polymers. Thus at 300°C polypyromellitimide devised from 9,9-bis-(*p*-aminophenyl)fluorene withstands a load of 500 kgf cm^{-2}, while at 400°C it withstands a load of 200 kgf cm^{-2}.

Polyimides obtained from dinuclear and polynuclear tetracarboxylic acids with phthalimide groups (Table 6, polymers Nos. 6–20) have a high heat resistance (although lower than that of polypyromellitimides), and their softening temperature can be regulated within wide limits by varying the nature of the bridging group between the phenyl rings of the tetracarboxylic acid or diamine residues[190,194].

Polyimides from aliphatic diamines show the lowest heat resistance among cardopolyimides but, even when the polymer chain contains long aliphatic fragments [$(CH_2)_6$ or $(CH_2)_8$], the softening temperature of the polymers reaches about 200°C.[78]

Like other polyimides, cardopolyimides have a high thermal stability[72,190] and in a series of polyimides thermal stability depends to an even greater extent on the nature of the cardo-group than among polyamides. Polyimides with fluorene and anthrone cardo-groups show the highest thermal stability[190,192]; on heating to 1000°C in an inert atmosphere (under the conditions of dynamic thermogravimetric measurements, the heating rate was 5 deg min^{-1}), they retain 68–70% of the weight of the initial specimen and the decrease in weight begins at 480–500°C.[72] The lowest thermal stability is characteristic of cardopolyimides with cyclohexyl groups[190,191], which, like aliphatic polyimides, begin to decompose in air at about 400°C. This has been explained by the initial degradation of the cyclohexyl groups. Polyimides with phthalide groups[72,190,191,201], the thermal stability of which is lower than that of the imide rings, occupy an intermediate position.

It has been shown that, at temperatures (300–350°C) preceding the onset of decrease in weight, processes leading to a change of molecular weight characteristics and solubility develop in polyimides[202].

Certain chemical properties of cardopolyimides (the data obtained are probably valid also for other polyimides) have been estimated. On heating, polyimides are resistant to acidolysis and exchange reactions involving the imide ring but decompose under the influence of amines and other bases[203,204]. Compared with the corresponding aromatic polyamides, polyimides are less resistant to hydrolysis[73,74]; their hydrolysis is accelerated in the presence of DMF, DMA, and DMSO[73,74] and depends on the chemical structure of the polymer and on its physical structure[196,205,206].

5. Poly-1,3,4-Oxadiazoles

Another class of heterocyclic cardopolymers are poly-1,3,4-oxadiazoles (Table 7). The use of aromatic dicarboxylic acids and their derivatives containing cardo-groups in the molecule for the synthesis of such polymers made it possible to obtain highly soluble amorphous polymers[71,73,86], poly[1,3,4-oxadiazole-2,5-diyl-1,4-phenylene-(3,3-phthalidylene)-1,4-phenylene] among which contains two phthalide groups per elementary polymer unit, shows the highest solubility; it is soluble in methylene chloride, TCE, DMA, HMP, NMP, pyridine, benzyl alcohol, etc.

The polydispersity of cardopoly-1,3,4-oxadiazoles synthesised in polyphosphoric acid has been estimated[208,209]. The polydispersity coefficient ($\bar{M}_w/\bar{M}_n$) of the linear poly-1,3,4-oxadiazole based on 3,3-bis-(*p*-carboxyphenyl)phthalide and its dihydrazide is 3.0–3.1. The variation of the viscosity of solutions of this polymer with molecular weight is of the following type[208]:

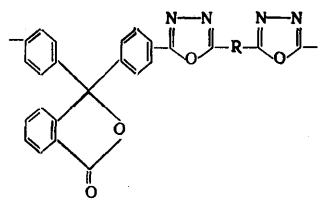
$$[\eta]^{25^\circ}_{DMA} = 7.74 \cdot 10^{-4}\,\bar{M}_w^{0.57},$$
$$[\eta]^{25^\circ}_{TCE} = 4.00 \cdot 10^{-4}\,\bar{M}_w^{0.66}.$$

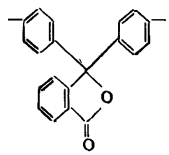
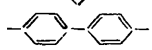
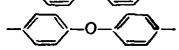
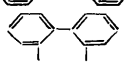
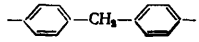
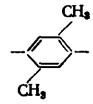
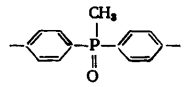
As in other cases, the introduction of phthalide cardo-groups into poly-1,3,4-oxadiazoles increases significantly the thermal stability of the polymer. Thus poly[1,3,4-oxadiazole-2,5-diyl-1,4-phenylene-(3,3-phthalidylene)-1,4-phenylene] softens at a temperature approximately 150 deg above that of amorphous poly(1,3,4-oxadiazole-2,5-diyl-1,4-phenyleneoxy-1,4-phenylene).[86]

Cardopoly-1,3,4-oxadiazoles are resistant at room temperature to the action of organic solvents, water, and

corrosive media; they are slightly degraded at elevated temperatures in amide solvents[210]. Poly-1,3,4-oxadiazoles are degraded at room temperature in 98% sulphuric acid[210]. The polymers have been found to be stable in water at 100°C; poly-1,3,4-oxadiazoles are hydrolysed at higher temperatures, the hydrolysis being accelerated in acid and basic media.

Table 7. Properties of cardopoly-1,3,4-oxadiazoles



№ №	R	$\eta_{int}^{25°}$, dl g^{-1}	d, g cm^{-3}	Softening temp.[b], °C	References
1		3.00	1.320	390	83,84
2		1.90	1.316	390	83,84
3		1.00	1.309	360	83,84
4		4.75	—	400	83,84
5		3.50	1.340	340	83,84
6		0.68	—	280	84
7		0.88	—	315	207
8		0.50	—	300	207
9		0.98	—	380	207
10	$-(CH_2)_8-$	1.66	—	160	207

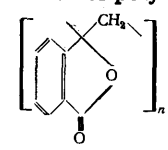
a. Concentration of polymer solution 0.5 g per 100 ml of TCE–phenol mixture (3 : 1 by weight).
b. See footnote b to Table 6.

Poly-1,3,4-oxadiazoles do not enter into exchange reactions involving the oxadiazole ring up to 200°C but decompose under the influence of carboxylic acids and their hydrazides.

Cardopoly-1,3,4-oxadiazoles obtained from 3,3-bis-(*p*-carboxyphenyl)phthalide begin to decompose in air according to dynamic thermogravimetric data obtained at a heating rate of 5 deg min^{-1} at 400–430°C, i.e. the thermal stabilities of the 1,3,4-oxadiazole and phthalide rings are approximately the same[194].

6. Carbon Chain Cardopolymers

Cardopolymers of the polymerisation type have been investigated in less detail, although the number of known examples of such polymers is very large. These include polyacenaphthylene[95,211–219], polyindene[85,220], polybiindenyl[221], poly(vinylene carbonate), poly(maleic anhydride)[100], polymaleimide[222], poly-*N*-phenylmaleimide[223,224], and polymethylenefluorene[225]. Systematic studies on carbon chain cardopolymers of methylenephthalide[93] and many methylenephthalimidines[94] and their copolymers with monomers of the vinyl type[1,226] have shown that such polymers are amorphous highly heat-resistant substances soluble in polar solvents. Thus polymethylenephthalide softens at about 300°C and dissolves in trifluoroacetic acid, formic acid, DMSO, the monohydrate of 1,3-dichloro-1,1,3,3-tetrafluoroacetone, trifluoroethanol, sulpholane, NMP, DMF, tricresol, etc., the solvent depending appreciably on the molecular weight of the polymer. It is distinguished from the majority of carbon chain polymers by a high density (d = 1.3462 g cm^{-3}). In a study of the glass temperatures of the copolymers of methylenephthalide with styrene, methyl methacrylate, and methyl acrylate, it was shown experimentally and by calculation[226] that the glass temperature of polymethylenephthalide should be 370–380°C, but is not attained owing to the depolymerisation process at temperatures in excess of 300°C.[1] Consequently the heat resistance of polymethylene phthalide



(X)

surpasses that of the majority of other carbon chain polymers and many heterochain polymers (polyarylates and aromatic polyamides).

The heat resistance of the carbon chain cardopolymers polymethylenephthalide, polymethylenefluorene, and polymethylenephthalimidine is independent of the chemical structures of the cyclic groups and is determined in this instance by the nature of the bonds in the main polymer chain[1,94]. All these polymers are depolymerised at temperatures in the range 250–300°C, while heterochain cardopolymers with similar groups remain thermally stable up to 350–450°C, the thermal stability of the latter depending on the nature of the cardo-groups (see above).

Comparison of the cardopolymers and other carbon chain polymers showed that the presence in the macromolecule of phthalide or phthalimidine groups improves the solubility of the polymer (for example, compared with polyethylene) in highly polar solvents[93]. However, the above carbon chain polymers do not dissolve in many polar solvents incapable of intense intermolecular association (for example in *sym*-tetrachloroethane) in which polystyrene dissolves readily, although it is insoluble in highly polar solvents such as trifluoroacetic and formic acids and DMSO. Such differences between the solubilities are probably due to the greater rigidity of the cardopolymers compared with polystyrene and the presence in the former of highly polar groups capable of intermolecular interaction.

Polymethylenephthalimidine and also copolymers of methylenephthalide and methylenephthalimidine dissolve in formic and trifluoroacetic acids, i.e. in solvents capable of rupturing intermolecular hydrogen bonds, but are insoluble in amide and chlorinated solvents[94].

In contrast to the cardopolymers mentioned above, polymethylenefluorene does not involve in the known organic solvents, which may be due to a definite albeit slight ordering of the structure of this rigid-chain polymer.

IV. APPLICATIONS

Films of various cardopolymers have been obtained by casting from solution in various organic solvents. The high heat resistance and thermal stability of such polymers ensures the stability of the physicomechanical and particularly the dielectric characteristics of such films up to 300°C.[21,86,138,152,193,227,228] Highly heat-resistant fibres of cardopolyarylates and certain other cardopolymers, which have an isotropic amorphous structure with traces of crystallinity, have been obtained by extrusion from solutions[113,180]. The use of cardopolymers as varnish coatings for plastics, as binders for fibreglass, as antifriction self-lubricating materials, and other products is also promising[229-232].

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Institute of Organic Derivatives
of the Elements, USSR Academy
of Sciences, Moscow

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Structure and Properties of Polymer Mixtures in Solution

V.N.Kuleznev and L.S.Krokhina

Modern views on the solubility of two polymers in a common solvent are discussed, and the possibility of controlling the properties of polymer mixtures is examined. A list of 125 references is included.

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I. INTRODUCTION

Mixtures of polymers are attracting increasing attention not only for the solution of applied problems but also in connection with the theory of the compatibility (mutual dissolution) of polymers, which in the amorphous state have the structure of highly viscous liquids. The high viscosity of polymeric liquids impedes the establishment of equilibrium, and macroscopic phase separation does not take place in mixtures of polymers even if the mixture actually comprises two phases, whose separation is determined thermodynamically. This fact is very useful for applied purposes, as it has led to the manufacture of materials from polymer mixtures. Nevertheless, the considerable difficulties involved in determining the phase constitution of a mixture of polymers have been responsible for broadening investigations of their properties in solution, where the phase composition can be easily established, and also means may be available for examining the structure of each phase separately and of the mixture as a whole. Many generalisations have already been made on polymer mixtures in solution, although they have been investigated systematically in effect during the past two decades.

The convenience of the rapid establishment of equilibrium in work with solutions is complicated by many difficulties, resulting from the presence of the solvent, in assessing interaction between the polymers themselves. For this reason results for polymer–polymer interaction in a polymer–polymer–solvent system cannot at present be confidently transferred to the polymer mixture in the absence of solvent or even to a solution of the polymers in a different solvent. Determining the interaction parameters of polymers and the structural parameters of their binary mixture from results obtained for their solutions constitutes a most important task for the future.

The present Review is concerned mainly to summarise work on solutions of polymer mixtures whose macromolecules contain neither ionogenic nor strongly polar groups. Reviews on this topic are lacking both in the Soviet and in the foreign literature.

II. THERMODYNAMICS OF THE MIXING OF POLYMERS AND THEIR SOLUTIONS

1. Polymer–Polymer System

The spontaneous mixing of two liquids leads to the formation of a true, single-phase solution of one component in the other, provided that the process is accompanied by a decrease in the Gibbs function, i.e. that

$$\Delta G = \Delta H - T\Delta S$$

is negative. The spontaneous process ceases when $\Delta G = 0$, and the liquids then have limited miscibility. The direction of the change and the magnitude of ΔG are governed by the relation between ΔH and $T\Delta S$, the enthalpy of mixing ΔH being determined by the magnitude and sign of the heat of mixing, while the entropy of mixing ΔS represents the change in order of the system resulting from the intermingling of the molecules.

The change in the parameters can be calculated most easily for an idealised system. If the structure of the miscible liquids and that of the mixtures are regarded as completely similar, so that neither the volume nor the short-range order is affected by mixing, the change in entropy is determined by the increase in the number of ways in which the two kinds of molecules can be distributed in space. Calculation based on the lattice theory of solutions[1-3] yields the formula

$$\Delta S = -kn_1 \ln \frac{n_1}{n_1+n_2} - kn_2 \ln \frac{n_2}{n_1+n_2} \qquad (2)$$

where k is Boltzmann's constant, for the change in entropy accompanying the mixing of n_1 molecules of one liquid with n_2 molecules of another liquid. According to this equation the entropy of mixing of the liquids decreases with increase in molecular weight. In fact, the higher the molecular weight the smaller the number of molecules (n_1 and n_2) in unit volume. Decrease in the number of molecules involves a decrease also in the number of combinations in which the molecules can be arranged: i.e. the entropy of mixing decreases.

If the molar volume of an ordinary liquid of low molecular weight is taken to be 100 cm³, and the molar volume of a polymer as 100 000 cm³, calculation using (2) for the mixing of 1 cm³ of one simple liquid with 1 cm³ of another gives[4] $T\Delta S$ = 8.3 cal/2 cm³; the corresponding value for the mixing of 1 cm³ of a polymer with 1 cm³ of the simple liquid is 4.5 cal/2 cm³, and for the mixing of the same quantities of two polymers $T\Delta S$ = 0.0083 cal/2 cm³. We are concerned here with the formation of an ideal mixture, in which molecules of one polymer are surrounded by those of the other, to give a molecularly disperse system, in which fluctuations of concentration are absent. These results show clearly that the entropy of mixing of polymers is so small that it can be disregarded in the calculation of ΔG. The quantity $T\Delta S$ cannot affect the sign of ΔG, so that the change in the Gibbs function is determined by the sign of the change in enthalpy (heat effect).

The same lattice model of a solution will yield a formula for the enthalpy of the mixing of n_1 solvent molecules with a volume fraction φ_2 of a polymer

$$\Delta H = kT\chi_1 n_1 \varphi_2 , \tag{3}$$

in which

$$\chi_1 = \frac{z\,\Delta\omega_{12} x_2}{kT} \tag{4}$$

is a dimensionless parameter representing the excess energy of interaction in the solution, where $\Delta\omega_{12}$ is the energy of interaction of a solvent molecule with a polymer segment of the same size, z is the coordination number of the model lattice, and $x_2 = v_2/v_1$ (the molar volumes of polymer and solvent being v_2 and v_1).

On the basis of the Flory–Huggins theory[1-3] presented here, Flory[5], as well as Scott and Magat[6], obtained almost the same expression for the chemical potentials of the mixing of two polymers (2 and 3), which can be written

$$(\mu_2 - \mu_2^0) = \ln\varphi_2 + \left(1 - \frac{x_2}{x_3}\right)\varphi_3 + x_2\chi_{23}\varphi_3^2 , \tag{5}$$

$$(\mu_3 - \mu_3^0) = \ln\varphi_3 \left(1 - \frac{x_3}{x_2}\right)\varphi_2 + x_3\chi_{23}\varphi_2^2 , \tag{6}$$

where χ_{23} is a parameter of interaction of the polymers, μ the chemical potential of one polymer surrounded by the other, and μ^0 the chemical potential of the same polymer surrounded by like molecules. The critical conditions for the mixing of two polymers (i.e. the concentration and the interaction parameter at which phase separation ensues) were determined by Scott[7], who obtained expressions for these critical values:

$$\chi_{23c} = \frac{1}{2}\left(\frac{1}{\sqrt{x_2}} + \frac{1}{\sqrt{x_3}}\right)^2 , \tag{7}$$

$$\varphi_{2c} = \sqrt{x_3}/(\sqrt{x_2} + \sqrt{x_3}) , \tag{8}$$

$$\varphi_{3c} = \sqrt{x_2}/(\sqrt{x_2} + \sqrt{x_3}) . \tag{9}$$

In the particular case of a mixture of polymers having molecules of the same length ($x_2 = x_3 = x$) we find that $\varphi_{2c} = \varphi_{3c} = \frac{1}{2}$ and $\chi_{23c} = 2$. Substituting $\chi_{23c} = 2$ in Eqn. (4) yields the condition

$$z\,\Delta\omega_{23}/kT = \frac{2}{x} \tag{10}$$

for a mixture of polymers at the consolute point. When x is large, $\Delta\omega_{23}$ is small. With the high molecular weights of polymers, their already negligible interaction energy, i.e. negligible absorption of heat on mixing, will lead to phase separation. Thus in an ideal mixture of polymers phase separation occurs with the slightest endothermic change, and the insignificant positive change in entropy is unable to balance the increase in enthalpy. The mixing of polymers can take place only with considerable evolution of heat.

A systematic investigation of the heats of mixing of polymers was first undertaken by Slonimskii and his coworkers[8,9]. In only two of the twenty-one pairs of polymers that they examined (polybutadiene rubber mixed with polystyrene and with butadiene–styrene rubber) was the sign of the thermal effect inconsistent with the behaviour of the polymers on mixing. The evolution of heat on the mixing of these two segregating pairs of polymers was attributed to a change in volume accompanying mixing.

Subsequent work has shown that segregation of a mixture of solutions or melts occurs even when the polymers are closely similar[10-14]. Two-phase systems appear in a mixture of melts of linear and branched polyethylene[15], in a mixture of solutions of the butadiene–nitrile copolymers SKN-18 and SKN-40,[16] in a mixture of melts of copolymers of methyl methacrylate and butyl acrylate whose macromolecules differ by more than 10% in their content of the former monomer[17], and also in a mixture of butadiene–styrene copolymers differing in composition by ~20%.[18] Two-phase systems appear even in a solution of a mixture of isotactic and atactic poly(methyl methacrylate) (so called stereocomplexes)[19]. There are grounds for expecting incompatibility of fractions of the same polymer differing significantly in molecular weight, which has already been shown for a solution of fractions of polyethylene[20].

Allen et al.[21] determined several thermodynamic functions of the mixing of oligomeric polyisobutylene and polymethylsiloxane. They measured the heat of mixing of the polymers experimentally, and calculated the interaction parameter per segment $\alpha_{23} = \chi_{23}/v$ (where v is the molar volume of the polymer) from the Flory–Huggins theory by means of Eqn. (3). The result was comparable in order of magnitude with that calculated on the basis of Hildebrand's theory from the difference between the solubility parameters δ_2 and δ_3 of the polymers. Since the latter theory assumes a random distribution of molecules, the result would correspond to a similar structure of the mixture. The value of α_{23} was equated to α_{23c}, which according to Eqn. (7) defines the condition of critical separation of the mixture into two phases. This permitted the critical temperature of mixing of the polymers to be calculated. If the heat of mixing had alone been responsible for the phase separation of this mixture, separation would have occurred at a temperature almost 300 deg below the observed consolute temperature. It was concluded[21] that the entropy contribution to the term $\chi_{23}kTn_1\varphi_2$ in Eqn. (3) is quite large. The entropy of mixing which they calculated from the experimental results differed considerably from the theoretical value. This discrepancy, a consequence of some ordering of the system, was regarded as responsible for the deviation of calculated values from experimental data.

Flory[22] has recently used Prigogine's theory of solutions[23] to calculate the changes in thermodynamic parameters accompanying the mixing of polymers. The equilibrium properties of a liquid—its thermodynamic functions—depend on the fluctuation of its density: i.e. they are determined by its internal structure. Mixing may involve changes in structure, which influence the thermodynamic functions. The structure of a liquid was characterised in terms of the density, the free volume, and also the coefficient of thermal expansion. Experimental values of the thermodynamic functions for polyisobutylene and polymethylene were used to calculate the

thermodynamic parameters of the mixing of these polymers at temperatures above the melting point. Thus $\Delta H = 2.5$ cal/100 g mixture at 150°C, while $T\Delta S$ is negative (−5.4). Therefore ΔG is large and positive (7.9), which indicates that the polymers are incompatible. Flory did not indicate reasons for the decrease in entropy on mixing. A possible increase in the degree of order of the system—an increase in short-range order—probably increases the non-combinatorial component of the entropy[24], which will be discussed in Section III.

The considerable decrease in entropy observed when polymers are mixed above the glass point shows that phase separation can occur even with a small exothermic effect, as has been found experimentally[8,9]. From the above it is obviously illegitimate to estimate the mutual solubility (compatibility) of polymers from the difference in their cohesion energies[25], for this disregards the important part played by the entropy factor in the expression for the free energy of mixing of polymers.

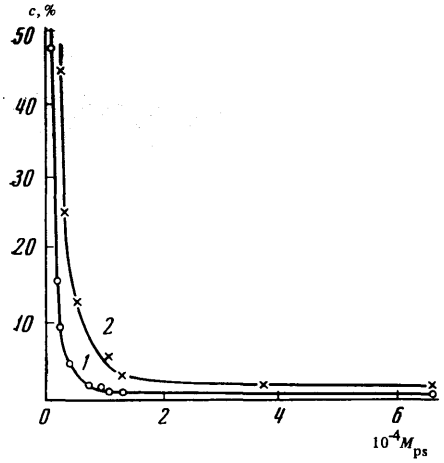


Figure 1. Solubility limit c (%) as function of molecular weight of polystyrene (ps) in: 1) polyisoprene ($\overline{M}_W = 10^6$); 2) poly(methyl methacrylate) (0.87×10^5).

The difficulty of the direct experimental measurement of the free energy of mixing demonstrates the importance of the direct determination of the mutual solubility of polymers[26,27] as a measure of their affinity. Fig. 1 shows that at high molecular weights the solubility of polymers is small (fractions of 1%) independently of their chemical nature: only at low molecular weights does the solubility increase. Polystyrene dissolves completely in polyisoprene of high molecular weight only when $M_W \leq 600$, and in poly(methyl methacrylate) when $M_W \leq 1500$.

These results are qualitatively consistent with those of other investigators. Thus Berek[28], while determining the variation in the critical separation concentration of polystyrene and atactic polypropylene in solution with polymers of different molecular weights, found by extrapolation that, in the absence of a solvent, complete miscibility was exhibited by polymers having molecular weights in the range 330—660. Kuhn and Cantow[29] found that poly(methyl methacrylate) of degree of polymerisation 17 ($M_W \simeq 1500$) should be a θ-solvent for polystyrene. Oligomeric acrylates of various structures display considerable solubility in poly(methyl methacrylate)[30].

The above work together with that of Paxton[31], who established the limited miscibility of oligomers, disproves predictions[32] that polymers having $M_W \simeq 10^4$ are completely miscible. Fig. 1 indicates that $M_W = 10^4$ is the molecular-weight limit below which solubility increases rapidly with decrease in molecular weight.

Poly(vinyl chloride) and the butadiene—nitrile rubber SKN-40, which interact strongly owing to the polarity of their groups, probably constitute the only pair of polymers of high molecular weight that differ in chemical nature but yet are completely miscible[33].

Since mutual solubility increases markedly (up to complete miscibility) as the molecular weight of polymers falls below $M_W = 10^4$, segmental solubility of polymers was postulated[34] at their interface. This phenomenon is due to the dual nature of the macromolecules: they actually consist of segments, which accomplish the elementary act of thermal motion (displacement of the macromolecule). Mutual dissolution of the segments of unlike macromolecules can be assumed to occur[34] at the boundary of block polymers and especially in solution. Mutual solubility of the segments is well supported by the complete miscibility of the monomers (even when hydrogenated) of most polymers. Further confirmation is provided by the good miscibility of oligomers (Fig. 1). Hence most polymers are macromolecularly incompatible, but segmentally compatible in the interfacial layer[34]. The presence of such a transition layer, resulting from segmental solubility, is evidently responsible for the quite intense interaction of polymers in two-phase mixtures, i.e. when they are incompatible. Experimental determinations of the free energy of polymer mixtures, recently begun by Tager[35], show that ΔG is quite large and negative even for a mixture of incompatible polymers.

2. Solvent—Polymer—Polymer (1—2—3) System

Under certain conditions solutions of mixtures of two polymers in a common solvent, completely miscible with each of the polymers, separate into two phases each containing predominantly one polymer. Experience has shown that separation occurs not only in mixtures of polymers differing markedly in nature and structure, whose mutual insolubility is self-evident, but also in mixtures of polymers which are very similar in nature, such as polymeric *o*- and *p*-methylstyrenes[36], linear and branched polystyrenes[10], poly(methyl acrylate) and poly(ethyl acrylate)[11], poly(methyl acrylate) and poly(methyl methacrylate)[11], etc.

At infinite dilution, when the solution contains isolated macromolecules, the polymer—polymer—solvent system forms a single phase. Like any critical phenomenon, phase separation results from the interaction of macromolecules of the same kind and the consequent change in the supermolecular structure of the system. On increasing the concentration of solutions of polymer mixtures, therefore, we may expect phase separation only at a sufficiently high concentration, as follows from Eqns. (7)—(9), depending primarily on the interaction parameter of the polymers χ_{23} and on their degrees of polymerisation x_2 and x_3.

The conditions for the transition of a single-phase solution into two phases have been analysed thermodynamically mainly by Scott[7], Tompa[37], and Maron[38]. The calculations by Scott and by Tompa, which are complementary, are based on the Flory—Huggins theory, and have

been reported in detail in the books by Flory[39] and by Tompa[40].

If we assume that the polymers have the same degree of polymerisation and the same affinity for the solvent ($x_2 = x_3 = x$ and $\chi_{12} = \chi_{13} < 0.5$), the equality of the chemical potentials of the polymers and the solvent in the two phases of the separated solution will yield (Eqn. 5) the formula

$$\ln \varphi_2 + \chi_{23}(1-v_1)\varphi_3^2 = \ln \varphi_2' + \chi_{23}(1-v_1)\varphi_3'^2 \qquad (11)$$

where the volume fraction of polymer 2 in one phase is $\varphi_2 = v_2/(v_2 + v_3)$ and its volume fraction in the other phase

$$\varphi_2' = \frac{v_2'}{v_2' + v_3'} = \frac{v_2}{v_2 + v_3} = 1 - \varphi_2$$

so that $\varphi_3 = 1 - \varphi_2$ and $\varphi_3' = 1 - \varphi_2'$. Equation (11) is fundamental, giving the composition of the coexisting phases of the separated polymer–polymer–solvent (2–3–1) system.

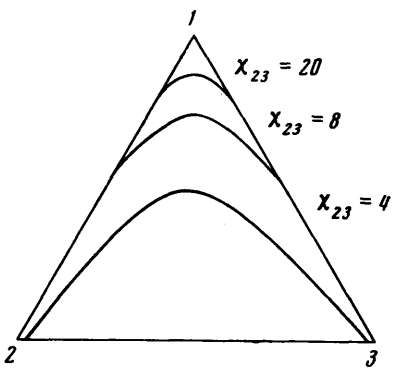


Figure 2. Diagram of solvent–polymer–polymer (1–2–3) ternary system with $x_2 = x_3 = x = 1000$ and the same interaction of the polymers with the solvent[7].

The "symmetry" of Eqn. (11) appears natural with the given initial conditions of equal degrees of polymerisation and the same affinity of the polymers for the solvent. Calculation of the phase diagram by means of Eqn. (11) yields symmetrical binodal curves separating the two-phase from the one-phase region (Fig. 2). In this case the position of the binodals is determined solely by χ_{23} and x.

By analogy with the binary system it is easy to determine the critical phase-separation concentration and the critical interaction parameter of the polymers in the ternary system:

$$\varphi_{2c} = \varphi_{3c} = (1 - \varphi_{1c})/2, \qquad (12)$$

$$\chi_{23c} = 2/(1 - \varphi_{1c}). \qquad (13)$$

Equation (13) shows that phase separation takes place only as a consequence of polymer–polymer interaction: the quantities χ_{12} and χ_{13}, representing the interaction of each polymer with the solvent, do not even occur in the equations for the critical conditions. Comparison of the critical interaction parameters of the polymers in ternary and binary systems (Eqns. 13 and 7 respectively) indicates that stronger interaction is tolerable between the polymers, without causing phase separation, in the presence of a solvent than in the binary system. As in the binary system, however, interaction between the polymers at the consolute point is small, as follows from an analysis of Eqn. (13). Equating χ_{23} from Eqn. (4) to the critical interaction parameter from Eqn. (13), we obtain

$$\chi_{23c} = xz\,\Delta\omega_{23}/kT = \frac{1}{1 - \varphi_{1c}},$$

which can be more conveniently written $\chi_{23c}(1 - \varphi_{1c}) = 1/x$. Hence χ_{23c} is very small for compounds of high molecular weight, corresponding to large values of x. It was therefor concluded that mutual insolubility of polymers in solution is the rule rather than the exception. The equation shows also that the larger the interaction parameter the lower the phase-separation concentration (Fig. 2). No phase separation takes place when $1 - \varphi_{1c} \ll 1/x$. Hence solutions of mixtures of polymers in which x is large should separate at very low concentrations, and the limit of separation should become lower with increase in the molecular weight of the polymers.

Scott showed[7] that a phase equilibrium diagram similar to Fig. 2 holds for a large class of ternary systems in which χ_{12} does not greatly differ from χ_{13}, while the length of the molecular chains satisfy the condition $x_2^{1/2} < x_3 < x_2^2$. Most systems encountered in practice conform to this condition, so that mutual insolubility of polymers in solution is general in character.

The symmetry of the phase diagram is destroyed if the equality $x_2 = x_3 = x$ does not hold. Unsymmetrical diagrams have been obtained[40-42] in which the consolute point was displaced in the ternary diagram (Fig. 2) along the axis of the polymers towards the polymer of lower molecular weight.

An unsymmetrical phase diagram is obtained also when $\chi_{12} \neq \chi_{13}$. The macromolecules are solvated to different extents, so that the actual sizes of the coils of macromolecules of different polymers differ even when they have the same molecular weight. No detailed thermodynamic analysis has been made of the effect of the nature of the solvent on the critical conditions of phase separation. However, Tompa showed[37] that, when there is no interaction between one of the polymers and the solvent, the phase diagram is completely unsymmetrical.

Thermodynamic analysis shows that polymers possess little affinity for one another. Thus from the solubility parameters of polystyrene and polybutadiene Scott[43] found that mixtures of two butadiene–styrene copolymers should segregate if their styrene contents differ by only 8%.[18] Tompa[40,42] predicted from his theory of phase equilibria that fractions of the same polymer might separate if they differ significantly in molecular weight and are placed in a poor solvent for the given homologous series of polymers. This deduction has since been confirmed experimentally[20,44].

According to theory[7] a completely incompatible system, i.e. a system in which one phase consists of solvent plus polymer 2, and the other of solvent plus polymer 3, is in principle possible only where χ_{23} is very large or at high concentrations of the polymers, which is quite well confirmed experimentally.

We now realise that the theories of the phase composition of a polymer mixture in solution are oversimplified, representing idealised views on the behaviour of polymers in solution. Nevertheless, the theory gives a correct view of the main features of phase separation in the polymer–polymer–solvent system, as is indicated by several experimental investigations reported below.

The main conclusions from the Flory—Huggins theory are supported qualitatively by the work of Dobry and Boyer-Kawenoki[45], who examined 78 combinations in solution. They studied the effect of the nature of the polymers, their molecular weights and proportions in the mixture, and also the type of solvent on the miscibility of the polymers in solution by determining the phase-separation limit and analysing the composition of the coexisting phases.

Theory has been confirmed also by investigations of a mixture of homologous polymers in a common solvent. Sieglaff[10] observed the separation into two phases of a mixture of a linear polystyrene with its microgel in benzene. The best quantitative support for the theory was provided by Koningsveld and Staverman[20], who calculated, in conformity with Tompa's predictions[40,42], that a third phase must be expected at 119.0—121.7°C in a solution of a mixture of two polyethylenes having molecular weights M_w of 1.2×10^4 and 5.4×10^5. Mixtures of these homologues in diphenyl ether actually separate into three phases in the range 120.4—121.6°C: the agreement with theory is entirely satisfactory. Shultz and Flory[46], who also investigated the phase separation of two polystyrene homologues ($x_2 = 770$ and $x_3 = 1100$) in cyclohexane, found that theoretical and experimental curves were of the same character, but the latter covered far wider ranges of composition and temperature. Koningsveld and Staverman[44] showed that the discrepancy was due to neglect, in Shulz and Flory's treatment of the experimental results, of the multimolecular character of the polymers.

Experimental work by Bristow[47] and by Berek et al.[28] provided quantitative confirmation of the theory. The former obtained symmetrical diagrams for the natural rubber—poly(methyl methacrylate)—benzene system and the latter for the polystyrene—polypropylene—toluene system; in both cases the polymers had the same molecular weights and a good solvent for both polymers was employed. The systems were analogous to the case examined by Scott[7] and characterised by the parameters $x_2 = x_3 = x$ and $\chi_{12} = \chi_{13}$. The consolute points calculated by Bristow did not lie on the experimental curves, which he attributed to inaccurate determination of molecular weights. The theoretical binoidal calculated by Berek by means of Scott's equation (11) coincided with the experimental curve. The symmetry was destroyed when polymers having different molecular weights were taken.

Allen et al.[32] made an interesting comparison of the Flory—Huggins and Hildebrand theories. They determined the interaction parameter $\alpha_{23} = \chi_{23}/v$ from the distribution of the polymers in the phases. The parameter found from the phase equilibrium was of comparable order of magnitude with the interaction parameters of other pairs of polymers, e.g. with that calculated by Scott[7] from Dobry and Boyer-Kawenoki's results and with that found by Stockmayer and Stanley[48] by light scattering. The interaction parameter was also calculated by means of Hildebrand's formula[49,50] $\alpha_{23} = (\delta_2 - \delta_3)/RT$. It is interesting to compare this work[32] with that of Paxton[31], who determined the interaction parameters of polymers by means of an equation, obtained by him on the basis of Maron's theory[38,51,52], for a mixture of two polymers of low molecular weight in a common solvent. This theory modifies the usual Flory—Huggins formula for the free energy by including a term representing the variation in the effective volume of the polymer in solution, as a consequence of which the interaction parameter varies with the concentration of the solution.

Table 1 assembles values of the interaction parameters, calculated on the basis of various theories, for polystyrene and polybutadiene in solution. The difference in the results given by the Flory—Huggins and Hildebrand theories is to some extent understandable. As already mentioned, Hildebrand assumed a completely random distribution of the molecules. The low results given by the Flory—Huggins theory indicate some ordering of the system and a decrease in entropy. This is confirmed by Flory's calculations for a binary system[22]. Nevertheless, the excessively high values of α_{23} obtained from Maron's theory, which already allows for some orientation of the molecules in the mixture, are completely incomprehensible, and Paxton's explanations of the discrepancies in α_{23} in terms of the polydispersity of the specimens are unconvincing.

Table 1. Polystyrene—polybutadiene interaction parameter calculated on basis of different theories.

Theory	α_{23}, litre^{-1}	Ref.
Flory-Huggins	0.1	32
Hildebrand	0.15	32
Maron	28—29	31

The results surveyed show that the Flory—Huggins theory provides the most complete description of the behaviour of ternary systems, although certain discrepancies are found, mostly concerning estimates of the interaction parameter of polymers in solution. According to the theory χ_{23} represents the energy of contact between segments of the two polymers, and is constant for a given pair of polymers, independently of the composition of the mixture and the temperature. Experiment shows that the interaction parameter depends on the mixture composition[32] and on the total concentration of polymers in solution[28]. Theory indicates also that χ_{23} is independent of the solvent, although in several cases it has been found to vary with the nature of the latter[36,53].

A need has undoubtedly grown in this field for general papers that will show, on the basis of comprehensive experimental data, the dependence of the limit of phase separation, the composition of the layers after separation, and ultimately the dependence of the structure of the polymer mixture after removal of solvent on the interaction parameter calculated by any available method.

III. ONE-PHASE SOLUTIONS OF MIXTURES OF POLYMERS

Nuclei of a second phase appear in any system long before the phase transition takes place. This should apply also to solutions of polymer mixtures, where corresponding changes in the supermolecular structure of the solution must be expected at concentrations below the phase-separation limit.

Association complexes of the macromolecules appear in a polymer solution at a certain concentration[24,54]. In a solution of a polymer mixture there are two theoretical

possibilities: either molecules of polymer A and those of polymer B can associate separately; or mixed adducts, each containing macromolecules both of A and of B, can be formed. In the former case increase in size of the association complexes with increase in concentration can reasonably be expected, terminating in the formation of an interface between unlike aggregates and the separation of droplets of a new phase. In the latter case increase in size of adducts of unlike macromolecules can hardly lead to separation of the solution into two phases, since experiment shows that, after a solution has separated into layers, each phase contains predominantly one of the polymers, so that adducts of unlike molecules must have broken down at the instant of phase separation, after which separation into layers occurs with the formation of association complexes of like molecules in each phase. The second type of structural changes at the instant of phase separation is illogical to the extent that formation of adducts of unlike macromolecules can probably be assumed only in cases in which the polymer mixtures do not separate into layers at all (at least in solution).

Although these suggestions on the mechanism of structure formation appear convincing, they require experimental verification, and the present Section is devoted to the relevant results.

When the concentration of a very dilute solution of a polymer is increased, a point may be reached at which isolated coils of macromolecules come into mutual contact. This ensues at a critical concentration c_1, indicated by a break on the property—concentration curves for the polymer solution[55,56] or determinable, following Debye, from the reciprocal of the intrinsic viscosity, the latter having the dimensions of a specific volume and characterising the density with which the solution is filled with macromolecule segments[57].

A critical concentration has been detected experimentally in solutions of polymer mixtures[58-60]. Cragg and Bigelow[58,59] determined the intrinsic viscosity and the intrinsic asymmetry ($[\eta]_A$ and $[\varepsilon]_A$) of a polymer A from light-scattering data in a solvent—a solution of polymer B of concentration c_B—and observed at the critical concentration a discontinuity—a peak or a dip—in the dependence of $[\eta]_A$ and $[\varepsilon]_A$ on c_B. Kuleznev and his coworkers[60] compared the intensity of scattering $R_{90}{}^{\circ\prime}$ by a mixture of polystyrene and polyisobutylene in toluene with the scattering by polystyrene in pure toluene, and found that, up to a certain concentration c_1, polystyrene scatters with the same intensity in the mixture as in pure toluene, after which its scattering in the mixture increases sharply. Such comparison was made possible by the isorefractivity of polyisobutylene and toluene, as a consequence of which the former was optically invisible in the latter. The critical concentration c_1 was easily determined from the break in the linear dependence of $c/R_{90}{}^{\circ\prime}$ on c. The considerable increase in intensity of scattering by polystyrene in mixtures having $c > c_1$ is attributed by the Reviewers to the fact that, in the presence of another polymer, the polystyrene macromolecules are constrained to associate to a greater extent than in the pure solvent (excess association).

The results reveal at least two characteristic concentrations in solutions of polymer mixtures, separating concentration ranges differing in structure. The first and lowest concentration may be c_1, at which the macromolecules come into mutual contact; at the second concentration c_2, termed the phase-separation limit, the solution divides into two layers. The concentration range c_1—c_2 gives solutions with a definite extent of association of the macromolecules: association begins at c_1, and at c_2 the size of the aggregates reaches a limit at which an interface appears (Fig. 3). Let us examine the changes in structure undergone by solutions of polymer mixtures within these concentration ranges.

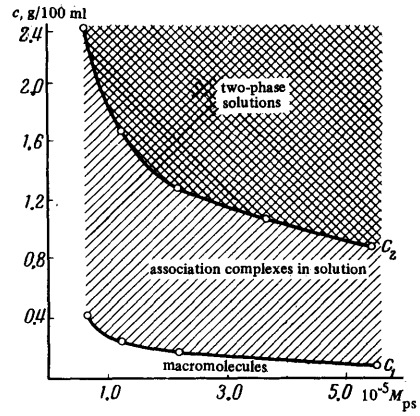


Figure 3. Concentration limits of solutions of polystyrene—polyisobutylene (7 : 3) mixtures in three structural states as function of molecular weight of polystyrene.

In 1964 we first proposed[61] the "polymeric" (isorefractive) solvent method for investigating such structures. The method consists essentially in choosing a solvent in which the increment of the refractive index of one polymer is zero, and a solution of this polymer of given concentration is used as the "polymeric" solvent, e.g. a solution of polyisobutylene in toluene. This permits the preparation of solutions of polymer mixtures, e.g. with different concentrations of polystyrene and a constant concentration of polyisobutylene. Such solution may be concentrated with respect to the polymer mixture, but dilute with respect to polystyrene, which permits the theory of dilute solutions and the usual methods of processing experimental results to be applied to the solution of polystyrene. The Debye or Zimm method can be used to determine the molecular weight of polystyrene, the size of its coil, and the second virial coefficient in a polymeric solvent at a different concentration. This principle has since been applied by several workers in investigating light scattering[29,62-65] and viscosity in solutions of polymer mixtures[53].

Using a very dilute polymeric solvent, Eskin[64] and Kuhn[62,63] observed a contraction of the polymer coil relative to its size in the pure solvent, but Kuhn noted that the coil is larger in a polymeric θ-solvent than in a θ-solvent of low molecular weight. Eskin[66] also remarked on the lack of identity between the two types of θ-solvents. The coil contracted with increase in concentration of the polymeric solvent, but, as already noted, the concentration remained low. Similar results were obtained in viscosimetric measurements[53], when a decrease in intrinsic viscosity with increase in the concentration of the polymeric solvent was established. However, these results are inconsistent with those of Hyde and Tanner[65], who found that the size of the polymer coil was independent of the concentration of the polymeric solvent, and attributed

this to the almost zero interaction parameter of the polymers. The Reviewers have shown[60] that the size of the coil of one polymer in a solution of another polymer remained constant over a certain concentration range of the polymeric solvent not exceeding the concentration at which association begins. At higher concentrations the coil size increases while the molecular weight remains constant. The Reviewers offer the explanation that, at solution concentrations below c_1, unlike macromolecules may be sufficiently far apart not to interact strongly enough to increase the extent of association or change the shape of the coil. If the concentration of the polymeric solvent comes to exceed c_1, the molecular coils of unlike macromolecules may interpenetrate. This is entirely possible, for the solution is a single phase at these concentrations, so that there is no physical boundary between coils of unlike molecules or their association complexes in contact. Thus a considerable concentration of segments of one polymer may be produced within a coil of the other polymer in a single-phase solution of a polymer mixture. Because contacts between like segments are preferred, the interaction of unlike segments will be equivalent to repulsion. As a consequence of the presence of polyisobutylene segments both outside and inside the polystyrene coil, the latter may either uncoil or contract depending on whether the resultant effect is directed inside or outside the coil. In the present case the polystyrene coil unwinds, becoming larger, a prerequisite for the association of such an "uncoiled" molecule with similar molecules, as occurs at high polystyrene contents in the solution. In other cases[62-64] the polymer coil became smaller with increase in concentration of the "polymeric" solvent.

The partial straightening (uncoiling) of coils with increase in solution concentration is characteristic of all individual solutions of polymers (see e.g. Ref. 57, p. 102). If, however, a solution of one polymer is diluted with a fairly concentrated polymeric solvent (total solution concentration close to the phase-separation limit of the mixture), the solution of the first polymer will not break down into individual coils of macromolecules, as Kuhn and Cantow showed[62,63], but the polymeric solvent will contain aggregates of degree of association ~55. It is obvious that data on the variation in size of the coil give limited information on possible association processes, for almost all the experiments mentioned were made at high dilutions of the polymer whose molecular association was being investigated.

The 1964 paper already mentioned reported the determination of the second virial coefficient A_2 of polystyrene from light-scattering data in a polymeric solvent (a solution of polyisobutylene). It was found that A_2 for polystyrene dropped sharply, approaching zero, with increase in the polyisobutylene concentration[61]. Kuhn has since found[29] that A_2 may not only reach zero but even assume negative values. The higher the molecular weight of the polymer in the polymeric solvent, the lower its concentrations at which A_2 becomes zero.

A decrease in A_2 indicates deterioration of the solvent. Hence a solution of one polymer is a thermodynamically poor solvent for another polymer. In poor solvents the association of polymers is large, which sometimes may even lead to separation of the polymer as a new phase. It can reasonably be assumed that macromolecules of one polymer will show a greater tendency to associate in the presence of another.

The scattering of light has been used to investigate association phenomena[60]. With simple liquids the composition variation of the scattering is often non-additive. A positive deviation in the intensity of scattering above the additive value indicates[67] excess molecular association relative to the mean degree of association of the two liquids.

The polymer–polymer–solvent system is more complicated than a mixture of two liquids. It would have been completely unjustified to apply the additivity principle here, and therefore the investigation was made in the polystyrene–polyisobutylene–toluene system, in which the latter two compounds had almost the same refractive indices, so that scattering in the mixture was due mainly to polystyrene, whose scattering $R_{90°}''$ was compared with its scattering in toluene. The dependence of $R_{90°}''$ on the composition of the polymer mixture (Fig. 4) at constant solution concentrations in the range c_1–c_2 passes through a maximum. The increased scattering by polystyrene in the mixture, relative to its scattering in toluene, depends on the proportions of the polymers, the molecular weight, and the concentration of the solution. The excess scattering $\Delta R_{90°}''$, obtained by subtracting the intensity of scattering by polystyrene in toluene from the intensity of scattering by the mixture, increases linearly with the concentration of the solution (Fig. 5), which separates into layers at concentration c_2.

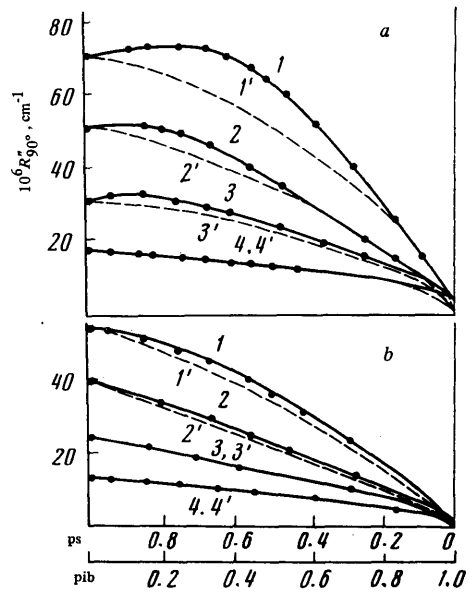


Figure 4. Dependence of $R_{90°}''$ ratio of polymers for polystyrene–polyisobutylene (ps–pib) mixtures in toluene solutions of constant concentration (g/100 ml): *a*) 0.5; *b*) 0.2 on molecular weight of polystyrene ($\times 10^{-5}$): 1) and 1') 5.5; 2) and 2') 2.2; 3) and 3') 1.2; 4) and 4') 0.65. The full (unprimed) curves represent solutions of mixtures, and the broken (primed) curves solutions of polystyrene.

The above results show that, in a solution of a mixture of polymers, like molecules begin to associate at a concentration c_1, and the association complexes reach their limiting size and density at point c_2, when the system separates into two phases. At the concentration c_2 the

density of association complexes of polymer A and polymer B is such that they acquire the properties inherent in particles of a new phase: in particular, a physical interface appears. It may be suggested that a polymer of given chemical nature will have a critical degree of association, independent of the molecular weight of the polymer, at which an interface is formed. This hypothesis was tested[80] by determining the excess scattering $\Delta R_{90°}$" by polystyrene of various molecular weights in mixtures having the same ratio of polymers (Fig. 5).

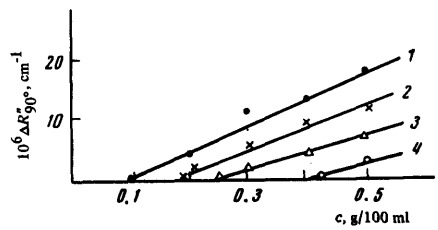


Figure 5. Concentration dependence of excess scattering $\Delta R_{90°}$" of polystyrene in mixture with polyisobutylene (7 : 3) in comparison with individual solution of polystyrene in toluene for different molecular weights ($\times 10^{-5}$) of polystyrene: 1) 5.5; 2) 2.2; 3) 1.2; 4) 0.65.

The excess light scattering can be regarded as the same in solutions of mixtures of polystyrene and polyisobutylene independently of the molecular weight of the former, provided that the solutions are in a corresponding state, i.e. that their concentrations are equidistant from c_1 and c_2. A dimensionless parameter—the reduced concentration $c^* = (c - c_1)/(c_2 - c_1)$, where c is the concentration of the solution of the polymer mixture in the usual weight units—was taken as measure of a corresponding state. The experiment showed that the dependence of $\Delta R_{90°}$" on c^* is represented by a single straight line for all solutions of mixtures of the two polymers in toluene, independently of the molecular weight of the polystyrene (Fig. 6). In the precritical range $\Delta R_{90°}$" is the same for all polystyrene fractions independently of their molecular weight.

It is hardly justifiable to assert that mixtures of different pairs of polymers will be represented by the same linear plot of $\Delta R_{90°}$" against c^*, since an interface is apparently formed at different densities of association complexes with different polymers. In any case, comparison of the tendency of polymers to associate in a mixture must obviously be made at equal values of c^*, whose calculation requires a knowledge of c_1 and c_2.

Thus a solution of a mixture of two polymers has a fairly specific "cellular" structure. Segments of polymer A are concentrated in individual microvolumes, and segments of polymer B in others; the intermediate spaces are filled with a mixture of segments of A and B in the absence of a physical interface. Light-scattering data show that microvolumes containing like segments (association complexes) are more densely packed than the corresponding homophase fluctuations in individual solutions of polymers A and B at the same concentrations by weight. Microvolumes containing a mixture of segments, on the other hand, would be loosened, for, in a system of incompatible polymers, the A—A and B—B segment interactions are more intense than the A—B interaction. Such a structure affects the properties of the solution, and also provides an explanation of certain aspects of the properties of polymer mixtures in bulk. Examples are given below.

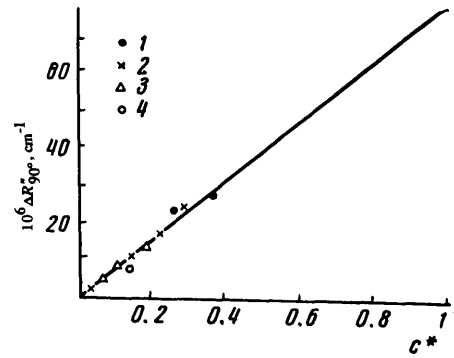


Figure 6. Dependence of excess scattering $\Delta R_{90°}$" by polystyrene in mixture with polyisobutylene on reduced concentration c^* for different molecular weights ($\times 10^{-5}$) of polystyrene: 1) 5.5; 2) 2.2; 3) 1.2; 4) 0.65.

The presence of microregions with a loosened structure leads to a considerable increase in solubility of a third polymer in a solution of a binary polymer mixture. If solutions are prepared of a mixture of polyisobutylene, polybutadiene, and polystyrene in chloroform having a total concentration of 4.0 g/100 ml but with different proportions of the polymers, the range of proportions in which the mixture is transparent defines the region of mutual solubility of the polymers. With the above total concentration of polymers in solution the solubility of polyisobutylene in polybutadiene and in polystyrene is ~1.4%, but its solubility in a 3 : 1 mixture of the latter polymers is 13%. Fig. 7 shows as example the solubility diagram for the polyisoprene—polyisobutylene—polystyrene system, where the effect is still more clearly evident.

A mixture of polyethylene and polypropylene illustrates the increase in order of arrangement of segments in each polymer phase when polymers are mixed in the melt[89]. The temperature range between the melting point and the crystallisation point in each polymer phase in the mixture is smaller than in the individual polymers. The fact that each molten polymer crystallises at higher temperatures in the mixture indicates a high degree of order in the molten mixture.

Research on solutions of polymer mixtures was first made by physicochemical methods, and the composition dependence of viscosity was studied initially. This approach was not altogether fruitful, for it was necessary to compare the viscosity—composition curve with the calculated or experimental curve for the same components forming an ideal mixture. The experimental curve then differs from the theoretical curve (ideal mixture), and the interaction of the components can be assessed from the magnitude and character of the deviations. Such approach is known to be fruitful for investigating the vapour pressure over mixtures of liquids of low molecular weight.

The situation is more complicated with polymer mixtures in solution, since in several cases the theoretical property—composition curve can be plotted only for very dilute solutions. For a long time the experimental curves were compared with straight lines connecting the properties of the individual components, which cannot be accepted as justified, since most properties—especially mechanical—are not represented by these lines even in ideal mixtures[70].

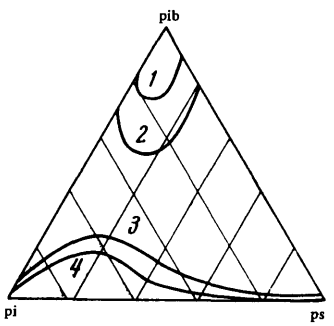


Figure 7. Miscibility diagram at 25°C for solutions of polyisobutylene (pib), polyisoprene (pi), and polystyrene (ps) in chloroform with different total concentrations (g/100 ml) of polymers in solution: 1) 2.5; 2) 2.25; 3) 2.25; 4) 2.5.[68]

It is very important here to examine the units in which the composition of the mixture is expressed and the quantity used to measure the given property. In fact Arrhenius long ago suggested, for the viscosity of binary liquid mixtures, the empirical formula[71]

$$\ln \eta = N_1 \ln \eta_1 + N_2 \ln \eta_2 \qquad (14)$$

where N_1 and N_2 are the mole fractions of the components, and η_1 and η_2 the corresponding viscosities. Although this formula is quite approximate, it nevertheless shows that viscosity is not an additive function of composition, but its logarithm varies linearly with mixture composition. For a polymer mixture this formula agrees with experiment only in the region of small concentrations[72].

Calculation of the composition dependence of a particular property can sometimes be usefully based on its dependence on molecular weight, since the molecular weight of a mixture is the mean of those of the components. Thus the calculation[73] of the dependence of the specific viscosity of a solution on the ratio of the polymers showed that mixtures of solutions of polyethylene fractions are not "ideal" even at low concentrations.

The intrinsic viscosity of solutions of polymer mixtures is given by the simple formula[74-78]

$$[\eta]_{m.} = x[\eta]_1 + (1-x)[\eta]_2 \qquad (15)$$

where x is the fraction of component 1 by volume[74-76] or by weight[77,78].

The specific interaction in solutions of polymer mixtures of finite concentration, at which unlike macromolecules interact, could be estimated if the ideal behaviour of the mixture were known. Thus several attempts were made to describe the theoretical specific viscosity η_{spm} of a solution of a mixture[73,79-81]. Krigbaum and Wall[79] suggested the formula

$$\eta_{spm} = [\eta]_1 c_1 + [\eta]_2 c_2 + b_{11} c_1^2 + 2\sqrt{b_{11} b_{22}}\, c_1 c_2 + b_{22} c_2^2 , \qquad (16)$$

$$b_{12} = \sqrt{b_{11} b_{22}} , \qquad (17)$$

where b_{11} and b_{22} are parameters of interaction between the like macromolecules, and b_{12} is the parameter of interaction between unlike macromolecules. An analogous equation, differing only in the expression for b_{12}, was proposed by Catsiff and Hewett[80]:

$$\eta_{spm} = [\eta]_1 c_1 + [\eta]_2 c_1 + b_{11} c_2^2 + (b_{11} + b_{22}) c_1 c_2 + b_{22} c_2^2 , \qquad (18)$$

where

$$b_{12} = \frac{b_{11} + b_{22}}{2} . \qquad (19)$$

Cragg and Bigelow[81] obtained a theoretical formula for the Huggins constant k' for a binary polymer mixture in solution and a theoretical value for the viscosity of the mixture:

$$\frac{\eta_{spm}}{c} = \frac{[\eta]_1 c_1 + [\eta]_2 c_2 + k_1' [\eta]_1^2 c_1^2 + k_2' [\eta]_2^2 c_2^2 + 2\sqrt{k_1' k_2'}\,[\eta]_1 [\eta]_2 c_1 c_2}{c_1 + c_2} . \qquad (20)$$

If the interaction parameter is taken to be $b = k'[\eta]^2$, this relation proves to be analogous to the Krigbaum—Wall equation.

These workers[79,80] propose that the difference between experimental and theoretical values of the parameter $\Delta b_{12} = b_{12,\,exp} - b_{12,\,theor}$ should be taken as a measure of the affinity of the polymers in solution.

Wright and Williamson[82] compared the two methods for calculating b_{12}, and considered that far better agreement between theory and experiment is obtained by substituting the arithmetic mean value of b_{12} in the appropriate equations.

The parameter Δb_{12} has recently been used to assess the compatibility of polymers in solution, and results have been obtained[41] coinciding with the estimate obtained from phase separation. Other workers[83] have shown that the range of compatibility of polymers can be established by means of Δb_{12}, but they regard the possibilities of the method as limited.

It is still impossible to calculate the composition dependence of viscosity (or a related quantity) at sufficiently high mixture concentrations. In some cases definite information can be obtained on the structure of a mixture of polymers in solution and on the intensity of their interaction by analysing the viscosity—composition curve itself, without comparing it with the curve for an ideal mixture[84,85].

Finally, it must be borne in mind, when plotting a property—composition graph, that the polymer macromolecules have different effective volumes in the solvent and in the mixed solutions. Mixing solutions of polymers in a common solvent usually involves an increase in the coil volume of that polymer which has the greater affinity for the solvent. It is then obvious that the true volume fraction of this polymer in the mixture will be larger than that calculated from the ratio of the initial volumes of solutions of equal concentration. The real volume ratio of polymers in a solution of their mixture has recently been allowed for[86].

IV. FACTORS INFLUENCING THE LIMIT OF PHASE SEPARATION

The more highly concentrated the solution of a polymer mixture at which it separates into layers, the broader the range of existence of thermodynamically stable single-phase systems. Although a polymer mixture is stable for an unlimited time in the absence of a solvent, and phase separation is prevented by the high viscosity of the components, the viscosity of solutions is usually sufficiently low for phase separation to occur quite rapidly and to be easily noticeable. Therefore study of the dependence of the phase-separation limit on various external and internal factors is an indirect method for assessing the effect of these factors on the compatibility of polymers in the block (in the absence of a solvent), where such estimates are very difficult. An investigation of this type is also of intrinsic scientific value in connection with the use of polymer mixtures as a common solution[87] for subsequent processing. The phase-separation limit of a solution of a polymer mixture can in principle be affected by the factors—(*a*) nature and structure of macromolecules, (*b*) proportions of polymers in mixture, (*c*) molecular weights of polymers and molecular-weight distribution, (*d*) type of solvent, (*e*) temperature, (*f*) shear stress, and (*g*) additives—which will be examined below.

(*a*) Nature and Structure of Macromolecules

A pair of polymers in solution can be regarded as compatible or incompatible depending on the concentration. The higher the phase-separation limit the higher the mutual affinity of the polymers, as is shown by experience, and the greater the compatibility of the polymers, it is usually supposed. However, the phase-separation limit of a mixture in solution is only a particular qualitative indication of the mutual solubility (compatibility) of the polymers. No comparison has been made of this limit or of its variation with the true solubility of the polymers in the absence of a solvent.

Analysis of published information shows[45,88,89] that solutions of polymers are usually mixed to establish the actual fact of their compatibility or incompatibility, without relating the phase-separation limit with their nature and structure. Polymers of apparently similar polarity, whether a mixture of two polar or two non-polar polymers, and also those differing strongly in polarity—a combination of polar and non-polar polymers—have been found to be incompatible[88,89]. Moreover, the incompatibility has been established of polymers of the same chemical nature, differing in the stereochemistry of the monomer units (the position of substituents[11,13]) or in the degree of chain branching[10,90]. Thus Kern[13] found that polymeric *o*- *p*-, and *m*-methylstyrenes were incompatible. Rylov and Karpov[12] observed mutual insolubility of natural rubber and gutta-percha, which are *cis*- and *trans*-isomers. Attempts were made to correlate the phase-separation limit with the structure of the polymers. Dobry and Boyer-Kawenoki[45] were unfortunately unsuccessful: no definite rule could be established.

In order to elucidate the effect just of the structure of the polymers, all factors influencing the phase-separation limit must be maintained constant, and only the chain structure of the macromolecules varied. This is an extraordinarily complicated task, since it is especially difficult to select polymers of the same molecular weight. Fuchs[11] was faced with this problem in studying the effect of the structure of polymethacrylates and polyacrylates on the limit. He determined the limit in benzene of solutions of mixtures of polyacrylates (methyl, ethyl, and n-butyl) with one another, mixtures of polymethacrylates differing in the length of the alkoxyl side-chain (methyl, ethyl, n-butyl, isobutyl, and hexyl), and also mixtures of polyacrylates with polymethacrylates, and compared the results with the difference in the number of carbon atoms in the monomer units of the mixed polymers. Unfortunately, the molecular weights were not always the same or even close, but nevertheless a general tendency could be established. A difference of one carbon atom, whether in the main chain or in a side-chain, was sufficient for the polymers to become incompatible. Thus poly(methyl acrylate) separated from poly(ethyl acrylate) and from poly(methyl methacrylate) in solution. Moreover, solutions of mixtures of poly(isobutyl methacrylate) with poly-(n-butyl methacrylate) separated into layers. The phase-separation limit fell with increase in the difference in the numbers of carbon atoms in the monomer units of the mixed polymers. Unfortunately, these rules were not verified on binary mixtures of two polymers in the absence of a solvent.

The effect of the degree of branching of the macromolecules on the phase-separation limit has also been studied[90].

(*b*) Proportions of Polymers in Mixture

The theoretically calculated binoidal separating the single-phase from the two-phase region in Fig. 2 shows that increasing the content of one of the components raises the phase-separation limit. This applies also to unsymmetrical diagrams. Regions having a low content of one of the polymeric components have in general been little investigated. Moreover, it has been noted several times[70,85,91] that phase separation does not take place when the mixture contains 10% of one of the polymers. This conclusion is probably due to the technique used to study the phase separation of solutions: solutions of the same concentration, deliberately exceeding the phase-separation limit for a 1 : 1 mixture, were always mixed in various proportions. But this concentration might be insufficient for the mixture to separate into layers when the content of one of the polymers is small.

A correct choice of technique enabled the Reviewers[92] to observe phase separation in a mixture of polyisobutylene with only 0.4% of polystyrene. It is quite obvious that the compatibility of a solution of one polymer with a solution of another depends on the total polymer concentration, and diminishes with increase in the total concentration of the solutions taken.

(*c*) Molecular Weights of Polymers

Dobry and Boyer-Kawenoki[45] were long ago able to establish qualitatively that the higher the molecular weight the lower the concentrations at which solutions separate into layers. Theory also predicts a decrease in mutual solubility with increase in the molecular weight of polymers.

The effect of molecular weight on the phase-separation limit has repeatedly been examined experimentally, and this usually ended in establishing empirical relations

unconnected with theory. Berek et al.[93] found the relation—later confirmed[94]—between the critical phase-separation concentration c_c and the molecular weights of the polymers

$$c_c = A(\bar{M}^+)^{-2/3} + c_\infty , \quad (21)$$

where $\bar{M}^+ = (M_i M_j)^{0.5}$ is the geometric mean of the molecular weights, M_i and M_j are the molecular weights of polymers i and j, and A and c_∞ are constants for a given pair of polymers. This equation applies in effect both to monodisperse and to relatively polydisperse polymers. Only when a combination of polymers is investigated whose molecular weights differ very markedly, and for which the conditions $\chi_{12} - \chi_{13} < 1$ and $x_2^{0.5} < x_3 < x_2^2$ are not satisfied, do the values of c_c depart from a linear dependence on $(\bar{M}^+)^{-2/3}$.

Berek's equation is similar to an equation proposed by Kuhn et al.[95]. Later results[29] indicate that the dependence of c_c on the molecular weight of polystyrene in the ternary system with poly(methyl methacrylate) and benzene is given by the equation

$$1/[\eta]_{nc} = a_1 \ln(c_c v_{av.}) + f(\bar{M}_{w_{nc}}) , \quad (22)$$

where v_{av} is the mean specific volume of the polymer, and a_1 and f are constants. An analogous equation can be written for the dependence of c_c on the molecular weight of the poly(methyl methacrylate).

On the assumption that the phase-separation limit should depend on the molecular weight and the type of solvent, Fuchs[96] suggested the empirical relation

$$\left(\frac{\eta_2}{P_2} + \frac{\eta_3}{P_3}\right) b = k c_3 , \quad (23)$$

where η_2 and η_3 are the specific viscosities of solutions of the polymers (c = 1 g/100 ml), P_2 and P_3 are the degrees of polymerisation of the polymers, and b and k are constants. The validity of this relation was confirmed on several pairs of polymers.

Analysis of the above results shows that decrease in molecular weight of the polymers (over the range investigated) was always accompanied by a rise in the phase-separation limit: i.e. the concentration range in which the solution consisted of a single phase increased.

(*d*) Type of Solvent

Theory regards the solvent as a simple diluent, which merely shifts the phase-separation limit.

Experimentally, Bristow's choice of solvents[47] was very unfortunate, one being a good solvent for both polymers, whereas the other was in our opinion a poor solvent, again for both polymers. He did not explain the effect of this quality on the symmetry of the phase diagrams, because he did not evaluate the quality, but simply started from the similarity in structure between solvent and polymers. At the present time no definite criterion of solvent quality is available, although certain properties of the solution have been correlated with solvent quality by Schulz[97] and by Tager[98,99]. As a consequence of the lack of a sensitive criterion for estimating the affinity of a solvent for a polymer, each worker has used his own criterion for assessing the quality of a solvent in investigating the effect of type of solvent on compatibility.

Kern[36] judged the quality of a solvent from its solubility parameter δ. He compared the parameters of various solvents with those of the mixed polymers, and observed maximum compatibility in solvents whose solubility parameters were closely similar to those of the polymers.

Fuchs[96] investigated the compatibility of polystyrene with poly(vinyl acetate) in eighteen solvents, in whose choice he was guided by the solvating power assessed from the viscosity of solutions of concentration 1 g/100 ml, which introduces some arbitrariness, as it would have been more reliable to base the comparison on the intrinsic viscosity. He determined the empirical relation (23), which indicates that the poorer the solvent (the lower the viscosity) the lower the concentration at which solutions separate into layers. This conclusion has been confirmed[27] on mixtures of widely varying composition, the quality of a solvent with respect to the polymers being judged from the intrinsic viscosity.

An explanation for the phase separation of a polymer mixture at lower solution concentrations the poorer the solvent is that polymer—solvent interaction is slight in poor solvents, so that polymer—polymer interaction increases. Deterioration in the quality of the solvent in the solvent—polymer—polymer (1—2—3) system involves an increase in the size of 2—2 and 3—3 polymeric association complexes. This size must probably reach a certain critical value for phase separation to ensue, and this occurs at a lower concentration in poor solvents because of the greater tendency of polymers to associate in such solvents.

Hugelin et al.[53] proposed that the affinity of a solvent for a polymer should be assessed by the constant α in the Kuhn—Mark—Houwink equation $[\eta] = kM^\alpha$, characterising the shape of the polymer coil, which varies with swelling. The phase-separation limit rises as the difference between the constants of the mixed polymers becomes smaller, except in poor solvents for both polymers. This is inconsistent with the results[27,96] indicating that the compatibility of polymers in solution diminishes as the quality of the solvent becomes worse. A poor solvent for both polymers should correspond to a small difference $\alpha_2 - \alpha_3$ and a low phase-separation concentration. Hugelin's equation evidently applies only to systems containing a good solvent for one or both polymers.

Sometimes homogeneous films can be obtained from a mixture of incompatible polymers by suitable choice of solvent. Thus Thies and his coworkers[100,101] obtained transparent and turbid films respectively of a mixture of polystyrene and poly(methyl vinyl ether) from solutions in toluene and in chloroform. The temperature dependence of the slope of the mechanical-loss curve indicates some microheterogeneity of the transparent films (one intermediate loss peak), but from the results there is no doubt about the strong effect of the nature of the solvent on the structure of the film.

(*e*) Temperature

Varied views have been published on the effect of temperature on phase separation. Several workers state that temperature has either almost no effect[62,63] or a very slight effect[28,45] on the phase-separation limit of solutions. Flory's theoretical calculation[22] of the thermodynamic functions of the mixing of polymers has also shown their independence of temperature. Other work[36,100] shows that temperature plays a considerable part, influencing the flexibility of the polymer molecules and also their solvation. Thus Kern[36] found that a mixture of polystyrene and poly(methyl methacrylate) in *o*-xylene separates into

layers at 25°C, and becomes a single phase at 85°C. In methoxybenzene, however, this mixture was homogeneous at 25°C, and separated at 85°C. A similar phenomenon was observed by Purcell[100] with a mixture of chlorinated rubber and an ethylene—vinyl acetate copolymer: the mixture was compatible at 25°C, but separated into layers with rise in temperature.

Available experimental results show that both lower and upper temperatures of mixing can exist in solutions of polymer mixtures, as in solutions of individual polymers. The more distant a solution from both consolute temperatures the less marked the effect of temperature on its phase constitution. Systems having a lower consolute temperature are evidently not a rarity among solutions of polymer mixtures. The desirability of further experimental investigation in this field is self-evident.

(*f*) Shear Stress

The phase-separation limit of solutions of polymer mixtures has been found experimentally to depend on the rate of stirring of the solution. Detailed studies have been made[86,102-104] of the effect of the rate of shear on the phase composition of a mixture of polymers in solution.

Silberberg and Kuhn showed[102] that, if the polystyrene—ethylcellulose—benzene system is subjected to shear, solubility of the phases equivalent to 15% dilution can be achieved at a certain rate of shear. The changes observed under the influence of a shearing force are completely reversible, in contrast to those occurring on dilution: the system again separates into layers immediately stirring ceases. Drops of an emulsion undergo deformation and breakdown in a field of mechanical shear stresses. Diminution in the size of the drops is associated with the accumulation of free energy in the system. The reverse phenomenon—coalescence and enlargement of the drops—accompanies the tendency of the free energy to decrease. Homogenisation depends on the relative rates of the two processes—destruction of the drops and their coalescence.

A more detailed investigation has shown[86,103] that, with increase in the shear stress, the phase-separation limit rises only to a certain limiting value, after which it ceases to depend on the shear stress. Thus c_2 in the polystyrene—polyisoprene—decalin system at 20°C increases from 10.5% to 12.5% with increase in the shearing stress ($\lg \tau$) from 1.2 to 2.9 dyn cm^{-2}, after which it ceases to depend on the stress.

Any pair of polymers can in principle be combined under shear, i.e. converted into a single-phase system, provided that the supermolecular structures in both polymers can be destroyed. Under these shear conditions in solutions of polystyrene and polyisoprene, however, the viscosity did not even reach that with limiting breakdown of the structure, which is indirect evidence of association of the macromolecules of each polymer in the system. This gave rise to the following explanation.

Previous Sections of the Review have mentioned that the macromolecules of polymers are incompatible, while their segments may be compatible, so that an intermediate layer is present at the boundary between the polymer phases. This layer is quite large in the absence of a solvent[105], and obviously becomes larger on addition of a solvent. As a consequence of the subdivision of droplets of a two-phase system under shear, their radius becomes close to the thickness of the transition layer even in the presence of comparatively coarse drops (according to Kuhn[102] amounting to micrometres or fractions of a micrometre). The system thus becomes a single phase while association of like macromolecules is preserved.

The above results must be taken into account in determining consolute temperatures and concentrations. Stirring the solution may lead to a change in the critical parameters, especially in very viscous systems.

(*g*) Additives

The compatibility of polymers in their mixed solutions can be influenced by additives of low molecular weight[84,91,106-108]. There is no generally accepted view on the mechanism of their action. Voyutskii et al.[84] attributed the action of polar additives—alcohol and acetone—on a mixture of solutions of poly(vinyl chloride) and a butadiene—styrene copolymer to the blocking of polar groups in the polymers by the additives. But this explanation did not fit the observed effect of methanol and acetone on a mixture of non-polar polymers[91]. Lipatov[106] explained the elimination of phase separation in solutions of polystyrene and poly(vinyl acetate) on the introduction of acetone by aggregation of the molecules and a change in their shape. However, Hunyar and Weisner[107], who investigated the effect of several simple substances on the poly(vinyl chloride)—cellulose nitrate—acetone system, found that phase separation was delayed by substances of higher surface tension than acetone or whose solutions in acetone possessed a higher surface tension than acetone itself. No quantitative relation was established between the concentration of additive eliminating phase separation and its surface tension.

Kuleznev and Igosheva[108] examined the effect of 23 additives representing various classes of chemical compounds on a polystyrene—poly(methyl methacrylate)—benzene mixture, and found that the phase separation of 9% solutions is completely eliminated by dimethylaniline, heptanol, and pentanol. There was no direct relation between the action of the additive and its surface tension, dipole moment, dielectric constant, or heat of evaporation.

We conclude by considering the action of copolymers and block copolymers on the phase separation of a mixture of the corresponding homopolymers[109,110]. There are no data to show that random copolymers or block copolymers raise the phase-separation limit of a mixture of homopolymers in solution. Block copolymers are stabilisers of the incipient emulsion of type "polymer A solution—polymer B solution". The size of the blocks controls that of the emulsion droplets[109,110]. Molau considers that a block copolymer acts as an emulsifier, forming a protective layer preventing adhesion of the drops of emulsion. We can hardly regard such explanation as satisfactory. Unlike blocks of the copolymer most probably form in a solution distinctive domains or, by analogy with soaps, micelles, in which the corresponding homopolymers undergo solubilisation, as is observed in the solubilisation of hydrocarbons in solutions of surface-active substances. Because the blocks are chemically combined in the block copolymer, and it is obviously impossible to separate the whole quantity of the latter into two macrophases, the emulsion remains stable. In our opinion it is also wrong to think that the effectiveness of a block copolymer is due merely to lowering the surface tension of drops of solutions of the homopolymers: the interfacial tension here by itself is negligible[111,112].

V. SOME ASPECTS OF THE TRANSITION OF A ONE-PHASE INTO A TWO-PHASE SOLUTION

The transition of a one-phase into a two-phase system has always been a central problem of colloid chemistry. Such a transition can conveniently be investigated on solutions of polymer mixtures, because the transition is produced by increasing the solution concentration: when a certain concentration c_2 is reached, the system separates into two layers—a solution of the less dense polymer above a solution of the denser polymer. The transition takes place here without change in chemical composition of the system, in particular without the addition of surface-active agents.

Very scanty data are at present available on the properties of a solution of a polymer mixture in the region of phase separation. In effect they relate only to the investigation of viscosity and light scattering[72,103,104,113].

The optical density of a system usually increases sharply in the vicinity of the phase-separation point, to reach a maximum at the instant of separation. After this the light scattering diminishes appreciably owing to the increase in size of the scattering particles and the non-monotonic variation in scattering with particle size.

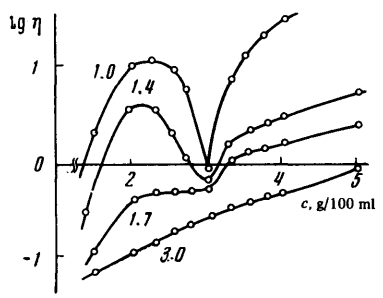


Figure 8. Dependence of viscosity on concentration of toluene solution of 1 : 1 polystyrene—polyisoprene mixture. The numerals on the curves indicate the shear stress ($\lg \tau$, dyn cm^{-2}) at which the solution was deformed.

The viscosity—concentration curve passes through a maximum before phase separation ensues. Fig. 8 shows such relations for different shear stresses[104]. Minimum viscosity corresponds to transition into a two-phase system. The minimum levels out with increase in shear stress, and at high stresses the viscosity increases monotonically with concentration: transition into a two-phase system is accomplished gradually over a wide concentration range.

The Reviewers accept the explanation that a polymer mixture may pass through a metastable region during the transition from a true solution into a rapidly separating two-phase system[57]. The region of metastable states may evidently be quite large in polymers, especially in view of their broad molecular-weight distribution. The structure of a polymer or its solution in the critical region has not yet been finally elucidated, and we can only make certain suggestions here. It is entirely possible that such compression of macromolecular coils or ordering of supermolecular structures occurs in this region that the viscosity decreases considerably. The possibility of such rearrangement is mentioned by Eskin[114], who calculated that the size of the macromolecular coils of a polymer is smaller by factors of 1.5—7 at the consolute point than at the θ-point.

Thus the most probable cause of the decrease in the viscosity of a solution of a polymer mixture in the region of phase separation is evidently the transition of the system into a special critical metastable state[115]. With increase in the variation in the shear stress, of course, fluctuating structures break, and separation of the solution into phases takes place gradually over a wider concentration range.

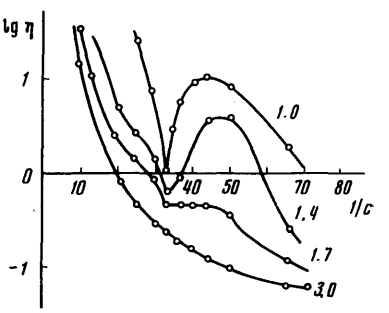


Figure 9. Dependence of viscosity of toluene solution of 1 : 1 polystyrene—polyisoprene mixture on the dilution $1/c$. The numerals on the curves indicate the logarithms of the shear stresses at which the solution was deformed.

It is interesting that the dependence of the logarithm of the effective viscosity on the dilution of the solution is represented by a family of curves (Fig. 9) resembling the isotherms of a real gas. The dilution axis expresses the volume occupied by 1 g of polymer, and the ln η axis can, though very arbitrarily, be compared with the pressure axis in a gas: like the pressure, the viscosity of a solution reflects the intensity of interaction of solute molecules. The function of different temperatures is filled here by different shear stresses, which, like the temperature in a gas, lead to the breakdown of association complexes. The greater the shear stress in a solution (or the temperature in a gas), the closer is the system to ideal. It is curious that the whole isostress line (line of equal shear stress), including the portion along which viscosity increases with dilution, can easily be obtained for a solution: the isotherm of a gas in the corresponding region (rise in pressure with increase in volume) cannot be obtained experimentally.

A decrease in the viscosity of a solution of a polymer mixture in the precritical region can be obtained also when the volume of one of the separating phases is very small. Thus the viscosity of a solution of a mixture of polystyrene and polyisoprene in decalin falls in the precritical range even when the quantity of polystyrene phase being formed is 2% of the total volume of the solution. This shows how specific is the interaction of polymers. This phenomenon can appropriately be compared with the effect of interstructural plasticisers on the viscosity of polymer melts[116]. It is significant that, in contrast to such plasticisers, the

addition of a solution of another polymer more viscous than the original solution may lower its viscosity. This is not due to a plasticising effect in the usual sense, but to the creation of conditions for transition into a special pre-critical state, in which the system as a whole has diminished viscosity.

VI. TWO-PHASE SOLUTIONS OF POLYMER MIXTURES

Insufficient study has been made of the structure and properties of solutions of polymer mixtures above the phase-separation concentration, which is easily understood from the instability of such systems with time. Two lines of information—the distribution of polymers and solvent in the separating phases and the rules of variation in interfacial tension between these solutions—are worthy of attention in this field.

Mixing solutions of different polymers in a common solvent, at a concentration above the phase-separation limit, produces a turbid emulsion of a solution of one polymer in a solution of the other polymer. The mixture is unstable: with time it gradually becomes clearer, and ultimately the mixture separates into two layers, between which a distinct boundary is visible. One of the layers is frequently more turbid than the other, and retains a cellular structure. The cause of the enhanced turbidity of one of the layers has not been studied. Each layer contains predominantly one polymer—the denser polymer in the lower layer, and the less dense in the upper layer.

The stability of a two-phase mixture of polymer solutions depends on the total concentration of polymers in solution, the composition of the mixture, and the temperature, as has been studied in detail by Mikhailov and his coworkers[117-119]. The stability was assessed visually from the appearance of an interface. The mixture became more stable with increase in concentration of the solutions, owing to the increase in viscosity. It had early been shown[45] that temperature has the opposite effect: it increases the rate of phase separation.

Theory predicts that each layer should contain predominantly one polymer, except in the vicinity of the critical phase-separation concentration. Each layer must contain a small amount of the second polymer. According to Scott's theory[7] complete incompatibility is possible only with very large interaction parameters or at high solution concentrations. At high concentrations, however, the kinetic stability, which is due to the high viscosity, increases strongly, and the establishment of equilibrium is retarded.

A detailed study of the composition of the layers was made on the polystyrene—atactic polypropylene—toluene system by Berek[28], who determined the concentration dependence of the polypropylene content of the mainly polystyrene lower layer, beginning from tenths percent above the critical concentration. Near the consolute concentration the polystyrene layer contained ~50% of polypropylene. With increase in concentration of the solutions the polypropylene content of the layer dropped sharply, to reach a value (4—5%) which remained almost unchanged with further variation in concentration. Calculation of the interaction parameter by means of Scott's equation showed that χ_{23} fell asymptotically with increase in concentration.

At first glance this contradicts Alekseenko's observation[120], on the system comprising polyethylene and a butadiene—styrene copolymer in a common solvent, that both polymers pass into the lower layer, only 4.8% of the copolymer remaining in the upper layer, whereas theoretically the latter should contain polyethylene. The probable reason is that polyethylene, which is sparingly soluble in the solvent at low temperatures, becomes insoluble in the presence of the second polymer, and is precipitated into the lower layer. The action of a second polymer in worsening the quality of a solvent for an initial polymer is well known[29,61-63].

On the basis that each layer contains predominantly one polymer, a method was proposed for determining the molecular weight of a polymer from the ratio of the volumes of the solutions resulting from separation of its mixture with a polymer of known molecular weight[45,106]. It was assumed that, when the two separated solutions are in equilibrium, the two phases have the same osmotic pressure. If each phase contains only one polymer, and the osmotic pressure is proportional to concentration, the molecular-weight ratios should approximate to the ratio of the concentrations of the polymers in the layers or to the ratio of the layer volumes. However, this method has not found application, since it does not allow for incomplete separation of the polymers, especially appreciable with polydisperse systems, and also disregards the effect of the nature of the solvent on the volume ratio. However, it may be of interest for a systematic estimation of molecular weight for a homologous series of polymers.

Lautout-Magat[121] made a general calculation of the partition coefficient of the solvent between the phases. The calculation was tested only on two polymer mixtures in solution.

Little study has been made of the establishment of equilibrium between the phases and of their composition. Available experimental results often concern only isolated aspects, and do not cover the phenomenon as a whole. For example, it was found[111] that, when solutions of the same concentration were mixed, the equilibrium concentration of the upper layer far exceeded those of the lower layer and of the initial solutions. However, no analysis was made of the composition of the polymer layers.

Hyde and Tanner[65] made an extremely interesting observation on the stability of the separated solutions resulting from mixing solutions of polystyrene and polyisobutylene in cyclohexane at 30°C, which is 4—5 deg below the θ-point of polystyrene in this solvent. Solutions of the mixtures were stable for several hours, and more concentrated solutions for several days. The polystyrene molecules were regarded as retaining the same ability to aggregate and be precipitated as in the absence of the other polymer, but their aggregation occurred extremely slowly in the mixture, as the solution contained polyisobutylene molecules.

The most important parameter characterising the properties of any two-phase system is its interfacial tension. As early as 1952 it was suggested[102] that a polymer—polymer—solvent system has a low value, because droplets of a solution of one polymer break down in a solution of another polymer at very low velocity gradients.

Among the first experimental determinations[111,112] were measurements of the interfacial tension between solutions of poly(vinyl acetate) and poly(vinyl chloride) in ethyl oxalate[111]. Two capillaries of different diameters were placed at the interface, and the tension was calculated from the difference in liquid levels in them. The extraordinarily low value of 10^{-3} dyn cm^{-1} was observed.

Interfacial tension has been determined also by the sessile drop method[112]. A drop of a solution of one polymer was forced out on to a solid support into a solution of

the other polymer. The interfacial tension could be calculated from the shape of the drop. At the interface between polystyrene and polyisobutylene solutions the tension was so small that the drop spread all over the support, and a considerable proportion was spontaneously dispersed in the surrounding solution of the other polymer.

Vrij[122] calculated the surface tension theoretically. The calculation of interfacial tension is formally similar to Debye's calculation of the scattering of light by polymer solutions near the consolute temperature. Vrij confirms directly that the two phenomena—separation of an individual solution of a polymer into layers at a critical temperature and phase separation of a mixture of solutions of incompatible polymers—are similar. The equation which he deduced is valid only for a symmetrical system, containing polymers of the same molecular weight. The calculated[122] interfacial tensions were of the same order of magnitude as the experimental values[111].

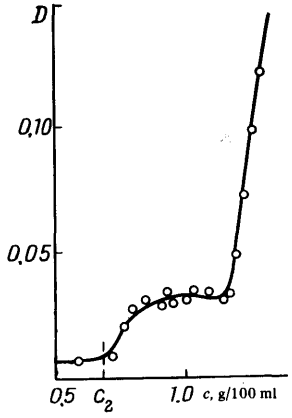


Figure 10. Dependence of optical density D on concentration c of toluene solution of polystyrene—polyisobutylene mixture.

The earlier work[112] was later continued[92] by measurements of the interfacial tension between solutions of polystyrene and polyisobutylene by means of two capillaries. With this pair of non-polar polymers, as with polar polymers[111], the interfacial tension tended to zero at c_2, and increased with increase in the concentration of the solution and in the molecular weight of the polymers. Values fluctuated within the range 0.01—0.001 dyn cm^{-1} depending on these two factors. Extrapolation to 100% concentration (absence of solvent) gave the interfacial tension between polystyrene and polyisobutylene as ~1 dyn cm^{-1}, the first experimental value of the interfacial tension between non-polar polymers of high molecular weight.

The low surface tensions can easily be explained by the presence of a considerable transition layer at the interface, resulting from the segmental solubility of polymers discussed in Section II.

Liquids of low interfacial tension are capable of spontaneous emulsification[123,124], when the increase in entropy of the system produced by dispersion exceeds the increase in surface [free] energy, so that the process occurs under the influence of the thermal motion and terminates in the formation of a thermodynamically stable two-phase system. This requires that the interfacial tension must have been <0.1—1.0 dyn cm^{-1}. Spontaneous mutual emulsification of polymers obviously cannot be observed in the absence of a solvent, owing to the high viscosity of the mixture. Nevertheless, the low polymer—polymer interfacial tension is one of the main reasons for the high operational compatibility of polymers[125].

Spontaneous emulsification of a drop of a solution of one polymer in another was observed as long ago as 1967,[112] and has since been studied in greater detail[92] on solutions of polystyrene and polyisobutylene. If a layer of a solution of the latter polymer is carefully placed on a solution of polystyrene, after a few weeks the upper layer will contain not only polyisobutylene but also 4.5—5% of polystyrene. The layer has become cloudy, and under a microscope drops of diameter 0.5—3 μm are visible. However, if the solutions are mixed, the concentration of the emulsion of the polystyrene solution in the upper layer is about 10% (weight of polystyrene to weight of polyisobutylene) after phase separation. Formation of a stable spontaneous emulsion in a polymer—polymer—solvent system can be observed also from the concentration dependence of optical density (Fig. 10), where the appearance of a stable emulsion corresponds to a horizontal portion on the curve.

The results explain the turbidity[45] of one layer after phase separation of a solution of a polymer mixture: it is due to formation of a stable emulsion of one solution in the other. It is interesting that, for a given pair of polymers in a common solvent, the cloudiness of the layer is determined by the viscosity ratio of the solutions: after phase separation the more viscous layer is turbid (Table 2).

Table 2. Phase separation of mixtures of solutions of polystyrene (ps) and poly(methyl methacrylate) (pmma) in a common solvent.

Mol. wt. M_w		Solvent	Parameters of true solutions			Cloudy layer
ps	pmma		c, g/100 ml	η, cP	η, cP	
$3.9 \cdot 10^5$	$0.87 \cdot 10^5$	benzene	20.0	604.4	37.5	upper
$3.9 \cdot 10^5$	$0.87 \cdot 10^5$	chloroform	20.0	536.8	33.0	upper
$3.9 \cdot 10^5$	$0.87 \cdot 10^5$	butyl acetate	20.0	495.2	27.2	upper
$3.9 \cdot 10^5$	$30.9 \cdot 10^5$	benzene	17.0	31.2	9 978	lower
$3.9 \cdot 10^5$	$30.9 \cdot 10^5$	chloroform	7.0	34.5	22 962	lower
$3.9 \cdot 10^5$	$30.9 \cdot 10^5$	butyl acetate	4.0	5.3	5 008	lower

The upper (polystyrene) layer is cloudy if its viscosity exceeds that of the poly(methyl methacrylate) solution; the lower layer becomes turbid if, owing to increase in molecular weight of the poly(methyl methacrylate), its viscosity exceeds that of the polystyrene solution. The effects of viscosity and the structural parameters of the polymers on the formation of stable emulsions is of great interest and requires further investigation.

Thus the vast majority of polymers are incapable of unlimited mutual dissolution, either in the presence or in the absence of a solvent. Segmental solubility occurs at the interface in their mixture, with a fall in interfacial tension to a negligible value. The low interfacial tension results in the spontaneous dispersion of a solution of one polymer in a solution of another; this is responsible for the high operational stability of a binary mixture of polymers. Within a certain concentration range below

the phase-separation limit, polymers in solution form a single-phase system generated by association complexes of macromolecules of the same chemical nature, the degree of association being greater than in a solution of the individual polymers of the same concentration. The association of macromolecules begins at the concentration c_1 and reaches a limit at the phase-separation point c_2; the degree of association is determined by the reduced concentration in the range c_1-c_2. The value of c_2 can be varied, and the concentration limits of single-phase mixtures increased, by varying the temperature, shear stress, nature of solvent, etc. The structural peculiarities of solutions of polymer mixtures lead to a sharp drop in viscosity in the concentration range directly preceding phase separation.

Further development of research on the theoretical and experimental thermodynamics of polymer mixtures is required, as a basis for comparing the interaction parameters of unlike polymers in solution and in the block.

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Lomonosov Moscow Institute of
Fine Chemical Technology

U.D.C. 547.496.3

Preparation of *N*-Substituted Thiourea

V.V.Mozolis and S.P.Iokubaitite

Results on the preparation of *N*-substituted thioureas by the reaction of organic isothiocyanates with compounds containing an amino-group, by the action of alkali-metal thiocyanates on amine hydrochlorides, and by the treatment of primary and secondary amines with thiocarbonyl chloride or carbon disulphide, published in the Soviet and foreign literature including 1972, are systematically discussed. The reactions of hydrogen sulphide with substituted cyanamides and of thiourea with compounds containing various functional groups are also examined. Certain views are presented on the mechanism of the formation of *N*-substituted thioureas, and the advantages and disadvantages of various methods for their preparation are compared. Practical applications of *N*-substituted thioureas are considered. A list of 247 references is included.

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I. INTRODUCTION

Thiourea is able to give both *S*-substituted and *N*-substituted derivatives. It was therefore thought possible that tautomeric transition into the thiol forms

$$-NH-\underset{|}{C}=S \rightleftarrows -N=\underset{|}{C}-SH$$

occurred in solutions of thiourea and its derivatives. However, the ultraviolet absorption spectra and Raman spectra of thiourea and its mono- and di-phenyl derivatives showed that the thione form was stable both in the crystalline state and in solutions, and no tautomerism was observed[1].

Since the time of the first syntheses of thiourea and its derivatives in the 1860s a vast literature has accumulated. The present Review is therefore restricted to methods of preparation and aspects of the practical application of *N*-substituted thioureas, and ignores metal-substituted derivatives and sulphothioureas. The literature up to 1954 is covered by specialised reviews on the chemistry of thiourea[2] and sulphonylthiourea[3], which emphasise specific aspects of individual methods of preparation and application of thiourea derivatives. The present Review has been guided by these surveys, and includes only a few of the literature sources cited. In every case, however, re-examination of these references has been dictated by a novel approach and the desire to preserve the integrity of the material reported.

The interest taken in thiourea and its derivatives can be explained by their wide applications: they have valuable pharmacological properties, exhibit insecticidal, fungicidal, and nematocidal activity, and are also widely employed as brighteners in the electrodeposition of metals.

II. METHODS OF PREPARATION OF *N*-SUBSTITUTED THIOUREAS

Methods of preparing *N*-substituted thioureas can be divided into six main groups.

1. Interaction of Organic Isothiocyanates with Compounds containing an Amino-group

The method consists in the direct interaction of organic isothiocyanates with compounds containing an amino-group, and can conveniently be used to obtain unsymmetrical thioureas. It can yield 1-monosubstituted derivatives[4-19]

$$RNCS + NH_3 \rightarrow RNHC(S)NH_2$$

1,3-disubstituted derivatives[4-9,11-13,17,18,20-167]

$$RNCS + R_1NH_2 \rightarrow RNHC(S)NHR_1$$

and 1,3,3-trisubstituted derivatives[7,10,17,18,34,35,37,42,49,58,68,77,79,89,105,145,160,168-178]

$$RNCS + R_1R_2NH \rightarrow RNHC(S)N\begin{matrix}R_1\\R_2\end{matrix}.$$

Various compounds containing an amino-group can be used for the preparation of thioureas by this method (Table 1), and various organic isothiocyanates can undergo this reaction (Table 2).

The condensation of organic isothiocyanates with amino-compounds is usually conducted in methanol or ethanol, but other solvents may also be used (Table 3). Papers have recently appeared on the possibility of carrying out the reaction in the absence of a solvent[49,71,83,106,116,140,141,153,164,170,171,176]. The process is

Table 1.

Amino-compounds	Ref.
Ammonia	4—6, 9, 11—19, 105, 154, 164
Chloral-ammonia	116
primary amines	
Saturated aliphatic	4—7, 11—13, 22, 34, 44, 47, 49, 54, 58, 59, 89, 105, 128, 135, 136, 140, 141, 144, 151, 154
Unsaturated aliphatic	16, 151
Aromatic	5, 6, 9—12, 17, 19—21, 23—28, 30—36, 38, 40, 41, 43, 50—57, 69—71, 89, 105, 108, 109, 134, 138—148, 150, 151, 154, 157, 159, 165—167
Heterocyclic	6, 8, 11, 12, 17, 18, 20, 21, 23, 25, 28, 32, 36, 50, 58, 74—80, 82—84, 86, 87, 90, 91, 94—107, 109—112, 115, 117—120, 123, 124, 138, 139, 144, 149—152, 155—158, 167, 171, 172, 177
Carbocyclic	6, 9, 46, 49, 59, 105, 109, 123, 124, 154
secondary amines	
Aliphatic	7, 10, 18, 34, 37, 49, 58, 89, 105, 145, 168, 169, 176
Aromatic	7, 17, 58, 105, 168, 176
Heterocyclic	9, 18, 37, 49, 72, 73, 77, 81, 85 86, 89, 92, 93, 104, 145, 168, 170, 178
Phenetidines	57, 62, 63, 88, 137
Hydroxylamines	161, 173, 174
Diamines	42, 45, 113, 114, 157
Amidines	162
Amides of carboxylic acids	74, 175
Amino-acids	39, 50, 54, 59, 121, 125, 126, 128—130, 158, 160, 165, 178
Esters of amino-acids	121, 122, 127, 131
Hydrazides of amino-acids	125
Lactones of hydroxy-carboxylic acids	132
Peptides	126
Amino-nitriles	133, 164, 175

Table 2.

Organic isothiocyanates	Ref.
Saturated aliphatic	4, 5, 8, 14, 20—22, 34, 35, 51, 53, 74, 75, 91, 92, 97, 98, 100, 106, 110, 112—114, 125, 131, 133, 136, 140, 152, 153, 157, 161, 162, 164, 168, 175, 176
Unsaturated aliphatic	8, 14, 23—28, 31, 32, 35, 62, 63, 70, 74, 75, 78, 79, 91, 97, 98, 110, 113, 114, 123, 124, 152, 153, 164, 171
Aromatic with saturated side-chain	5, 7, 8, 10, 14, 17, 27, 28, 34, 38—56, 60, 69—87, 90, 91, 93—103, 106—108, 110—113, 115—124, 127—130, 132—135, 137—144, 147—152, 155, 157—165, 167, 169—174, 176, 178
Aromatic with unsaturated substituents	6, 15, 16
Heterocyclic	10, 18, 76, 78, 79, 88, 89, 104, 105, 108, 120, 124, 139, 146, 156, 171
Saturated carbocyclic	75, 110, 113, 154, 161, 176
Unsaturated carbocyclic	11, 12
Acyl	13, 30, 32, 33, 36, 37, 39, 51, 56, 57, 60—66, 105, 157, 166
Aroyl	13, 57—59, 109, 123, 124, 126, 175
Carbamoyl	145
Cyanoalkyl	128

generally accomplished with cooling or at room temperature, sometimes with heating[4,6,8,9,12,15-17,20,21,23-26,28,30,34,36,38-41,43,44,51,52,55-57,60-63,65,66,70,71,72,74-80,82,83,85,86,88,90-108,111-113,115-117,120-122,125,127,129,134,135,137,140,141,143,144,147,149,151-153,157,158,160,163-165,167,169-171,173,175]. There are also exceptions to the usual equimolecular quantities of the reactants, when excess of the organic isothiocyanate[20,21,23-25,93,98,99,113,117,131] or excess of the amino-compound[5,7,29,48-50,96,104,105,117,170] is taken.

The usual products of the reaction of primary amines with isothiocyanates are unsymmetrical 1,3-disubstituted thioureas. However, there are indications[87,147,171] that the condensation of heterocyclic amines with aryl isothiocyanates gives ambiguous results on more prolonged heating: symmetrical 1,3-disubstituted thioureas are formed together with the unsymmetrical derivatives. Symmetrically substituted thioureas are probably products of secondary reactions of the initially formed unsymmetrical thioureas, cleavage of which leads to the accumulation

Table 3.

Solvent	Ref.	Solvent	Ref.
Acetone	9, 13, 17, 18, 30, 33, 43, 55, 56, 58, 61, 64—68, 109, 111, 117, 129, 130, 134, 135, 140, 157, 159, 164—166, 175	Toluene	32, 80, 92, 93, 131
		Dioxan	22, 31, 39, 117, 178
		Chloroform	80, 114, 140, 141
		Ethyl acetate	83, 148
Diethyl ether	5, 31, 39, 51, 52, 89, 110, 128, 156, 161, 162, 175	Acetonitrile	59, 99, 119, 120, 145
		Pyridine	34, 95, 98, 106
Petroleum ether	29, 140, 168, 176	Methylene dichloride	4
Benzene	6, 9, 13, 30, 33, 44, 45, 47, 57, 58, 62, 63, 75—79, 82—88, 91, 94, 96, 99, 101—103, 105, 107, 109, 117, 118, 126—128, 133, 141, 148, 149, 155, 157, 161, 163, 167, 168, 171, 174	Hexane	6
		Cyclohexane	48
		Acetic acid	54, 163
		Pentanol	106
		Water	4, 11, 37, 59, 140

of two different amines and two different isothiocyanates in the mixture, which then yield two symmetrical thioureas:

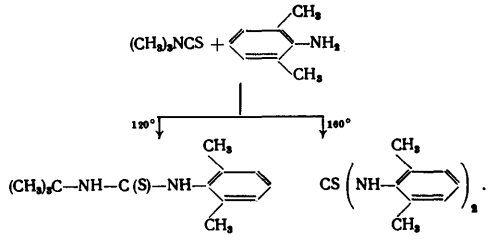
$$RNCS + R_1NH_2 \rightleftarrows \underset{(I)}{RNHC(S)NHR_1} \rightleftarrows RNH_2 + R_1NCS,$$

$$R_1NH_2 + R_1NCS \rightarrow I,$$

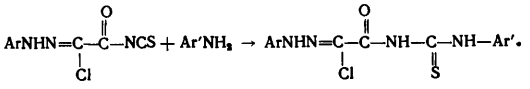
$$RNH_2 + RNCS \rightarrow RNHC(S)NHR,$$

The driving force of such changes is provided by differences between the basic strengths of the amines RNH_2 and R_1NH_2 and between the reactivities of amines and aryl isothiocyanates. The proportions of the products depend on the stability of the thiourea derivative formed initially.

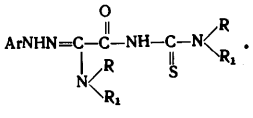
Aliphatic isothiocyanates react very slowly with aromatic amines, to form symmetrical or unsymmetrical 1,3-disubstituted thioureas depending on the temperature[140]:



Isothiocyanates of arylazochloroacetic acids react very peculiarly with amines. The isothiocyanate group interacts with the formation of 1-aryl-3-arylazochloroacetylthioureas[67,68]:



Also the chlorine atom is replaced by the amine residue[68] to yield thioureas of the type



2. Reaction of Alkali-metal Thiocyanates with Amine Hydrochlorides

Heating mono- and di-substituted ammonium thiocyanates at 160°C for a few hours brings about rearrangement into thioureas:

$$\underset{(II)}{RR_1NH_2SCN} \rightarrow RR_1NHC(S)NH_2.$$

Such rearrangement is impossible with tri- and tetra-substituted ammonium cations.

This rearrangement is used for the preparation of 1-monosubstituted thioureas[91,179-190]:

$$RNH_2 + HCl + NH_4SCN \rightarrow RNHC(S)NH_2 + NH_4Cl$$

and also 1,1-disubstituted derivatives[191,192]

$$RR_1NH + HCl + NH_4SCN \rightarrow II + NH_4Cl.$$

The method is straightforward, and can be used for aliphatic, aromatic[179-183,185,186,191,192], and heterocyclic[91,186-188] amines, esters of amino-acids[184], and diamines[189,190]. An example of the reaction with a diamine is the preparation of *N*-2′-aminoethylthiourea:[190]

$$KSCN \xrightarrow{5} H_2NCH_2CH_2NH_2 + HCl \rightarrow H_2NCH_2CH_2NH_2^+SCN^- \rightarrow$$
$$\rightarrow H_2NCH_2CH_2NHC(S)NH_2.$$

The reaction of alkali-metal thiocyanates with amines is usually conducted in an inert organic solvent, most frequently chlorobenzene[179,180,182,184] or in aqueous medium[181,183,185,186,189,190]. Other solvents—glacial acetic acid[187,188], methanol[191], and ethanol[191,192]—may also be used. Chlorobenzene is saturated with hydrogen chloride, the appropriate amine and the alkali-metal thiocyanate are added, and the mixture is heated at 110–120°C for a time depending on the nature of the components. When the reaction is conducted in water, hydrochloric acid, the appropriate amine, and a small excess of the alkali-metal thiocyanate are added, and the solution is boiled and evaporated to dryness. The residue is dissolved in an appropriate solvent, and then precipitated with hydrochloric acid. The saturation of chlorobenzene with hydrogen

chloride or the addition of hydrochloric acid to water can be avoided by using the amine hydrochlorides[179,180,182,183,185-189,191,192] or sulphates[180].

The yield of thiourea increases slightly with increase in the concentration of the reactants, but it remains low, since side-reactions occur with the formation of an isothiocyanate

$$RNH_2 + 2HCl + NH_4SCN \rightarrow RNCS + 2NH_4Cl$$

and a symmetrical 1,3-disubstituted thiourea

$$RNCS + RNH_2 \rightarrow RNHC(S)NHR.$$

In the reaction of 1 mole of ammonium thiocyanate with 2 moles of tryptamine hydrochloride, for example, 1,3-di-[2-(5-methoxyindol-3-yl)ethyl]thiourea is obtained[107].

This method can be used to prepare arylthioureas having either electropositive or electronegative substituents, and is considerably more convenient and rapid than the preparation of arylthioureas from aryl isothiocyanates and amines.

3. Reaction of Thiocarbonyl Chloride with Primary and Secondary Amines

Primary amines react with thiocarbonyl chloride to form, depending on their quantity, either isothiocyanates[19,193]

$$RNH_2 + CSCl_2 \rightarrow RNCS + 2HCl$$

or symmetrical 1,3-disubstituted thioureas[193-195]

$$2RNH_2 + CSCl_2 \rightarrow RNHC(S)NHR + 2HCl.$$

Secondary amines form only symmetrical 1,1,3,3-tetrasubstituted thioureas[196]:

$$2RR_1NH + CSCl_2 \rightarrow RR_1NC(S)NRR_1 + 2HCl.$$

In order to prepare thioureas by this method, 1 mole of thiocarbonyl chloride is heated with 2 moles of the amine in an aqueous[193,194] or in an aqueous acetone[195] medium.

The course of the reaction may be

$$RR_1NH + CSCl_2 \rightarrow \underset{(III)}{(RR_1NHClCSCl)} \rightarrow RR_1NCSCl + HCl.$$

If the compound (III) is stable, the reaction

$$III + RR_1NH \rightarrow RR_1NC(S)NRR_1 + HCl \qquad (a)$$

takes place independently of the nature of the radical R_1. If, however, (III) is unstable ($R_1 = H$), a different reaction takes place:

$$III \rightarrow RNCS + HCl,$$
$$RNCS + H_2NR \rightarrow RNHC(S)NHR. \qquad (b)$$

Primary amines are able to react with thiocarbonyl chloride in conformity both with (*a*) and (*b*), but secondary amines can undergo only reaction (*a*). The correctness of this mechanism is supported by the fact that in some cases compound (III) has been isolated from the reaction mixture and identified[196].

Owing to the toxic properties of thiocarbonyl chloride this method is very rarely used—only when other methods do not give the results to be expected, e.g. for the preparation of symmetrically 1,3-disubstituted thioureas containing strongly electronegative substituents.

4. Reaction of Carbon Disulphide with Primary and Secondary Amines

This method is most simply and generally applied to the preparation of symmetrical 1,3-disubstituted thioureas[38,40,52,71,90,97,142,167,182,188,196-208].

$$2RNH_2 + CS_2 \rightarrow RNHC(S)NHR + H_2S$$

Because of the great volatility of carbon disulphide, excess is used over the 1 mole per 2 moles of the amine indicated by the equation. The reaction is complete when the evolution of hydrogen sulphide ceases.

This method can be employed for the preparation of 1-monosubstituted derivatives[182]

$$RNH_2 + CS_2 \rightarrow \underset{(IV)}{RNHC(S)SH},$$
$$RNHC(S)SH + NH_3 \rightarrow [RNHC(S)S]^-[NH_4]^+ \rightarrow RNHC(S)NH_2 + H_2S,$$

unsymmetrical 1,3-disubstituted derivatives[208-210]

$$IV + R_1NH_2 \rightarrow [RNHC(S)S]^-[NR_1H_2]^+ \rightarrow RNHC(S)NHR_1 + H_2S,$$

and 1,3,3-trisubstituted thioureas[142,169,211]

$$IV + (R_1)_2NH \rightarrow [RNHC(S)S]^-[N(R_1)_2H_2]^+ \rightarrow RNHC(S)N(R_1)_2 + H_2S.$$

Carbon disulphide reacts with primary amines—aliphatic[199,202,207], aromatic[38,40,52,71,167,169,182,196-198,200,207,208,211], heterocyclic[39,90,97,167,188,199,201,209,210], and hydroxylamines[208]—to form symmetrical and unsymmetrical 1,3-disubstituted thioureas and with secondary amines—aliphatic[142,169,211] and cyclic[142]—to form 1,3,3-trisubstituted thioureas.

This method is not advisable with arylamines having strongly electronegative substituents, since the latter greatly lower the yields of thioureas, nor with heterocyclic amines, which react with carbon disulphide with very great difficulty.

Carbon disulphide reacts not only with primary and secondary amines but also with amino-acids[142,203-205] esters of amino-acids[204], dicyclohexylcarbodi-imide[199,200], and *N*-benzylbis-*p*-methoxyphenylmethanimine[212]

The solvent used is normally ethanol[38-40,52,71,97,142,167,169,182,188,196,197,201,202,210,211] or benzene[167,182,197], but sometimes methanol[205], water[203,206], diethyl ether[90,199,200], oxolan[199], pyridine[197,200,204], or dimethylformamide[208].

A substantial disadvantage of this method is its duration. Catalysts for the reaction are sulphur[38,97,142,167,197,201], hydrogen peroxide[197,207], caustic potash[40,52,167,188,196], caustic soda[198,203,205,206,209,211], pyridine[197,200,204], pyridine together with iodine[197,204], and potassium ethyl xanthate[39]. Sulphur accelerates the reaction, but difficulties arise in separating it from the reaction products. Hydrogen peroxide is an efficient catalyst, but in this case free sulphur is formed (from the carbon disulphide), which is difficult to remove.

The most practicable catalysts are caustic potash and caustic soda, which involve the intermediate formation of thiuram disulphides and isothiocyanates:

$$RNH_2 + CS_2 + NaOH \rightarrow RNHC(S)SNa + H_2O \rightarrow$$
$$\rightarrow RNHC(S)S{-}SC(S)NHR \rightarrow 2RNCS + H_2S + S. \qquad (a)$$

Thioureas are formed in subsequent stages of the reaction:

$$RNCS + NH_2R \rightarrow RNHC(S)NHR,$$
$$RNHC(S)S{-}SC(S)NHR \rightarrow RNHC(S)NHR + S.$$

If R = Alk, thioureas can be formed only in conformity with Eqn. (*c*), for an aliphatic isothiocyanate rearranges

rapidly into the corresponding amine, without having time to react with the primary amine.

Pyridine can also be used to accelerate the reaction. It forms unstable products with hydrogen sulphide. Still better results are obtained by adding to the solution of pyridine the calculated quantity of iodine, which is easily removed as pyridinium iodide:

$$2RNHI_2 + CS_2 + I_2 + 2C_5H_5N \rightarrow RNHC(S)NHR + 2C_5H_5N \cdot HI + S.$$

During the reaction the solution becomes decolorised, and pyridinium iodide is precipitated. The quantity of iodine is measured out very carefully, for excess will lead to formation of the corresponding isothiocyanate:

$$RNH_2 + CS_2 + I_2 + 2C_5H_5N \rightarrow RNCS + 2C_5H_5N \cdot HI + S.$$

Small quantities of potassium ethyl xanthate catalyse this reaction. Although the acceleration is less than with sulphur, purer products are obtained.

5. Reaction of Hydrogen Sulphide with Substituted Cyanamides

Thioureas are formed by the reaction of cyanamides with hydrogen sulphide. Monosubstituted cyanamides yield 1-monosubstituted thioureas[213,214]:

$$RNHCN + H_2S \rightarrow RNHC(S)NH_2.$$

Disubstituted cyanamides yield 1,1-disubstituted thioureas[14]:

$$R_1R_2NCN + H_2S \rightarrow R_1R_2NC(S)NH_2.$$

The reaction is best accomplished by saturating an ethanolic solution with the corresponding cyanamide, ammonia, and hydrogen sulphide, used either as a saturated solution[214] or in the gaseous state[14,213]. Ammonia acts as catalyst in this reaction. The reaction mixture is then boiled[213] or heated in a sealed tube at 100°C.[214]

At high pressures hydrogen sulphide can add also to dicyanodiamide to form amidinothiourea[215]:

$$H_2NC(=NH)NHCN + H_2S \rightarrow H_2NC(=NH)NHC(S)NH_2.$$

6. Reaction of Thiourea with Compounds containing Various Functional Groups

Since thiourea contains mobile hydrogen atoms, it will react with compounds having various functional groups to form mono-, di-, tri-, and tetra-substituted derivatives.

Quite a few papers have been published on the condensation of thiourea with aldehydes[216-226]. Thiourea can condense with formaldehyde both in equimolecular proportions to form hydroxymethylthiourea[216-218,221,225] and at a molar ratio of 1 : 2 to form bishydroxymethylthiourea[216-225]. This reaction has been conducted with 36.4%[219] and 40%[216,218] solutions of formaldehyde made alkaline with caustic soda[219] or baryta[216,218].

Mono-, bis-, and tetrakis-hydroxyalkylthioureas have been obtained by the condensation of thiourea with other aliphatic, alicyclic, aromatic, and heterocyclic aldehydes in molar proportions of 1 : 1, 1 : 2, and 1 : 4 in ethanol at pH 9:[226]

$$RCHO + NH_2C(S)NH_2 \rightarrow RCHOHNHC(S)NH_2,$$

$$2RCHO + NH_2C(S)NH_2 \rightarrow RCHOHNHC(S)NHCHOHR,$$

$$4RCHO + NH_2C(S)NH_2 \rightarrow (RCHOH)_2NC(S)N(CHOHR)_2.$$

1-Monosubstituted thioureas can also undergo condensation with formaldehyde at pH 7, to form unsymmetrical 1,3-disubstituted thioureas[227]. The condensation of unsymmetrical substituted thioureas with aldehydes in acid media yields the thioureas $RR'C{:}CH.NH.CS.NR'R'''$.[228]

Thiourea and 1-monosubstituted thioureas will condense not only with aldehydes but also with ketones, forming 1-monosubstituted[229,230] or unsymmetrical 1,3-disubstituted[230] thioureas.

Thiourea reacts with alkylphenols in the presence of concentrated hydrochloric acid in 37% aqueous formaldehyde solution to form bishydroxyalkylbenzylthioureas[231,232].

Thiourea will react with amines to form 1-aminothioureas[57,234] and symmetrical 1,3-diaminothioureas[57,233,234] respectively below and above 150°C. At high temperatures equilibrium is established between thiourea and ammonium thiocyanate:

$$NH_2C(S)NH_2 \rightleftarrows NH_4SCN.$$

The latter reacts with amines to form aminothioureas. 1-Monosubstituted thioureas yield unsymmetrical 1,3-disubstituted thioureas with amines[235]. Thiourea reacts with organic acids[236-238] or esters[239,240] to yield symmetrical 1,3-disubstituted[236,237] and unsymmetrical 1,3-disubstituted[238-240] derivatives.

Thiourea will react with mono- and di-arylated cyanamides[241], chlorides of carboxylic acids[242], and substituted propiolactones[243] to give 1-monosubstituted[241,243], symmetrical[241], and unsymmetrical[242] 1,3-disubstituted thioureas.

III. SOME ASPECTS OF THEIR PRACTICAL APPLICATION

N-Substituted thioureas have great preparative value for the identification of organic compounds, e.g. amines and organic isothiocyanates[2,144]. They are also able to form complex compounds with several metal ions. In this connection *N*-substituted thioureas are used in analytical chemistry as complexing agents[6,17,65,172,244,245].

Certain unsymmetrically 1,3-disubstituted thioureas exhibit biological[20,21,23,131], physiological[20,27,77-79,227,243], bacteriostatic[63,178], and bactericidal[35,50,110,166] activity, and find application in medicine.

Most *N*-substituted thioureas possess pharmacological properties[15,25,41,138,155], and therefore find widespread application as tuberculostatic[28,38,39,47,50,52-54,60,62,64-68,70,72-76,80,82,85,86,93,96-98,104,108,111,112,117,118,123-125,129,137,143,149-152,157,160,185,194,195,209,235], antineoplastic[51], antispasmodic[69], antitrichomonad[95], antiviral[112,154], and other[84,92,166,214] therapeutically active substances.

Descriptions have recently appeared of 1,1-dimethyl-3-[2,3(2,4)-dimethylphenyl]-2-thiourea[110] and a 3-substituted 1-(1,2,3,4-tetrahydroisoquinol-2-yl)alkyl-2-thiourea[169], both possessing hypotensive activity and used for the treatment of high blood pressure, and of 1,3-bis-*p*-aminophenylimidazolylthiourea[195], which exhibits chemotherapeutic activity and is employed in the treatment of cancerous conditions, chiefly leukaemia.

Several derivatives of allylthiourea[23-27] and phenylthiourea[41,127,159] find application as plant-growth regulators; and 3-substituted 1-hydroxythioureas[161] exert an inhibiting effect on certain microbiological systems.

Several *N*-substituted thioureas possess herbicidal[44,116,196,211,238], fungicidal[52,63,139,166,170], nematocidal[10], and rodenticidal[42,186-188] activity, and are used in agriculture against soil nematodes[10], insects[174], rodents[42,186-188], and other pests.

Derivatives of *N*-substituted thioureas are employed as protective agents against radiation[246] and are capable of enhancing the resistance of the organism to X-rays[69].

N-Substituted thioureas are widely used in industry as starting materials for the production of polymers[16,31], stabilisers of copolymers in polyalkenes[222], vulcanisation accelerators in the manufacture of porous rubbers[136,166], agents for whitening wool[223] and for impregnation of acrylonitrile[224], corrosion inhibitors[166,232], antioxidants[166,231], and brighteners in sulphate copper-plating electrolytes[225,247].

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Institute of Chemistry and
Chemical Technology,
Lithuanian SSR Academy of
Sciences, Vilna

U.D.C. 542+543-43

Advances in the Chemistry of Inorganic Films and the Interference Indicator Method

E.S.Vorontsov, V.K.Altukhov, A.N.Korneeva, and N.P.Peksheva

The fast developing field of chemical methods of preparation of inorganic films is reviewed, and a new method of investigating heterogeneous reactions (based on recent advances in the chemistry of inorganic films) is formulated, and termed the "interference indicator method". Specific features of the method are discussed, and examples are given of its application to studies of mechanism, kinetics, and catalysis in heterogeneous reactions; the limitations of the method, and its advantages and disadvantages, are also discussed. 106 references.

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I. INTRODUCTION

1. Inorganic Films on Solids

It has been known for a long time that the surface properties of solids can be improved by the application of inorganic coatings, which tend to prevent physical or chemical interactions between the solid and the surrounding medium and in this way extend the useful life-span of a large number of articles. Surface films on solids can also have decorative, protective, and complex physicochemical and electrophysical functions.

Interest in inorganic films has increased steadily during the last few years: for example, the publishing house "Mir" has produced the fifth (and almost certainly not the last) volume in the series "Physics of Thin Films" [1] during 1972. Whereas physicists are primarily interested in the physical and mechanical properties of thin layers of inorganic materials, chemists are concerned mainly with developing new and better methods of preparation of films having prescribed properties.

The increasing importance of thin films in science and technology stems not only from their decorative, protective, and mechanical properties when applied to everyday materials, but also from new developments in electrical and radio technology such as the microminiaturisation of integrated electronic circuits, which was made possible by the exploitation of thin films of metals, semiconductors, and insulators ("planar technology") [2,3].

The chemical composition of the films can be simple (single component) or complex (multi-component); their phase composition also can be simple (single-phase, homogeneous films) or complex (multi-phase, heterogeneous films). As regards electrical properties, we can distinguish metallic, semiconducting, and insulating (or dielectric) films. There is no generally accepted classification of the films in terms of thickness: for example, some workers [4] consider films between a monolayer and 100 Å in thickness as very thin, between 100 Å and 10 000 Å as thin, and above 1 μm as thick, whereas others [5] specify thin films (up to 400 Å), films of intermediate thickness (400–5000 Å), and thick films (over 5000 Å).

In this review we shall not be concerned with electroplated metal films, which are discussed systematically and in detail elsewhere [6]. The chemistry and technology of enamel films are also well known [7].

Chemical methods of preparation of thin films, relying on a wide range of reactions, have made considerable progress in the last few years. We have based our "interference indicator method" for the physicochemical study of heterogeneous chemical reactions [8-10] on these recent advances in the chemistry of thin films.

2. Chemical Methods of Preparation of Inorganic Films

The application of chemical reactions to the preparation of inorganic films is developing in the following directions.

1. The reaction between a solid and its gaseous or liquid environment, leading to the formation of a layer of product in whose composition the original solid is included. Oxide, sulphide, halide, and other films are produced on metals and semiconductors by this reaction. The method can be described schematically by the equations

$$A_{(s)} + B_{(g)} = AB_{(\text{film on A})}, \quad (1)$$

$$A_{(s)} + B_{(\text{soln.})} = AB_{(\text{film on A})}, \quad (2)$$

where $B_{(\text{soln.})}$ denotes a solution of B in any solvent.

For example, the oxidation of iron and its alloys in alkaline solutions and in water vapour is now widely used [11]. A salt-like film having strongly protective properties is formed when metals are phosphated [12].

The formation of oxide films on metals is described in detail in a number of monographs [13-18].

As a result of the development of semiconductor microelectronics, several papers on the growth of oxide films on Si and Ge have appeared in recent years. The preparation of films on silicon by oxidation in water vapour, in

dry or in wet oxygen, and also by anodic oxidation has been discussed by many workers[19-24].

2. The deposition of a film on a substrate, followed by chemical treatment to produce the desired properties. This method can be described schematically by the equations

$$A_{(film)} + B_{(g)} = AB_{(film)}, \quad (3)$$
$$A_{(film)} + B_{(soln.)} = AB_{(film)}, \quad (4)$$
$$AB_{(film)} + C_{(g)} = A_{(film)} + BC_{(g)}, \quad (5)$$
$$AB_{(film)} + C_{(soln.)} = A_{(film)} + BC_{(soln.)}. \quad (6)$$

For example, a metal film is deposited on a plastic, ceramic, alloy, or semiconductor, and it is allowed to react with a gas or a liquid to give an oxide, sulphide, selenide, telluride, halide, or more complex film.

On the other hand, one can deposit a layer of a compound on the substrate and convert it into a coating of simpler chemical composition by decomposing it or by allowing it to react with the surrounding medium. Copper–nickel coatings have been prepared[25-27] by reduction with hydrogen or carbon monoxide of mixed layers of Cu_2O and NiO, previously deposited on a ceramic or metallic substrate. This chemical procedure is interesting because it enables "hot" metallic coatings to be prepared without using molten alloy baths. Furthermore, the method is superior to electro-plating, which cannot provide complex metallic and metal-ceramic layers.

3. The most rapid progress has been made in the preparation of films by chemical deposition from the vapour phase. Reduction of a compound of the desired element, followed by condensation of the element on a substrate, is one important variant of this method:

$$AC + B = A_{(g)} + BC, \quad (7)$$
$$A_{(g)} = A_{(film)}, \quad (8)$$

where B is a reducing agent.

The growth of monocrystalline films of silicon on sapphire and on spinel ($MgO.Al_2O_3$) by reduction of $SiCl_4$ or decomposition of SiH_4, and the epitaxial relationships of the layer and the substrate, have been adequately discussed[28-37]. Silicon films offering the best crystallographic and electrical properties are obtained on sapphire previously heated to a high temperature in a hydrogen atmosphere.

Films of metals having a relatively high vapour pressure have been obtained[38] by chemical reduction followed by distillation and condensation at normal pressures, avoiding the need for relatively expensive vacuum equipment. The process can be described by the following equations:

$$MO_{(s)} + B_{(g)} = M_{(s)} + BO_{(g)}, \quad (9)$$
$$M_{(s)} = M_{(g)}, \quad (10)$$
$$M_{(g)} = M_{(film)}. \quad (11)$$

Many compounds (including oxides, sulphides, carbides, borides, silicides, and various intermetallic compounds) can be prepared by chemical vapour deposition. The reaction is usually carried out at atmospheric pressure. The growth conditions and the properties of the following films have been described: Si_3N_4,[39-47] rutile (TiO_2),[48,49] Ta_2O_5,[50] Nb_2O_5,[51] and Al_2O_3.[52-57]

We may consider the following reactions as typical of the chemical deposition of compounds from the vapour phase:

$$3SiCl_{4(g)} + 4NH_{3(g)} = Si_3N_{4(s)} + 12HCl_{(g)}, \quad (12)$$
$$2AlCl_{3(g)} + 3H_2O_{(g)} = Al_2O_{3(s)} + 6HCl_{(g)}, \quad (13)$$
$$2SiO_{(g)} + O_{2(g)} = 2SiO_{2(s)}. \quad (14)$$

In addition to reduction and oxidation, decomposition reactions can be used for chemical vapour deposition. Typical examples are:

$$Ni(CO)_{4(g)} \xrightarrow{200-300^\circ} Ni_{(s)} + 4CO_{(g)}, \quad (15)$$
$$SiH_{4(g)} \xrightarrow{800-1300^\circ} Si_{(s)} + 2H_{2(g)}, \quad (16)$$
$$CH_{4(g)} \xrightarrow{1000-2000^\circ} C_{(s)} + 2H_{2(g)}. \quad (17)$$

Involatile materials are commonly deposited by the procedure known as chemical transport. The term "chemical transport" denotes a process in which an involatile material is transported (in the form of a volatile compound) from one region of the system (called the source region) to another region (called the deposition or substrate region). The process consists of three steps: 1) conversion of the source material into a volatile compound by a chemical reaction; 2) transport of the compound to the substrate; 3) decomposition of the compound close to or directly on the substrate, and deposition of the source material on the substrate. For example[58]:

$$Ti_{(s)} + 2NaCl_{(g)} \rightarrow TiCl_{2(g)} + 2Na_{(g)} \quad (18)$$
$$TiCl_{2(g)} \rightarrow Ti_{(s)} + Cl_{2(g)} \quad (19)$$

Disproportionation reactions (in particular, of metal halides) are among the most widely used for chemical transport. They rely on the fact that many involatile metals can form an unstable, volatile, lower halide at high temperatures. Hence, when such a metal reacts with the higher halide at relatively high temperatures, the lower halide is formed, and the latter disproportionates to the metal and the higher halide when it reaches the lower-temperature region of the system. The metal is deposited on the substrate, and the higher halide is returned to the vapour phase, and can be transported back to the source region. This transport cycle can continue until the whole of the source material has been transported to the substrate. A known example of this process is the transport of silicon in the iodide system[59]:

$$Si_{(s)} + 2I_{2(g)} \rightarrow SiI_{4(g)}, \quad (20)$$
$$Si_{(s)} + SiI_{4(g)} \rightarrow 2SiI_{2(g)}, \quad (21)$$
$$2SiI_{2(g)} \rightarrow Si_{(s)} + SiI_{4(g)}. \quad (22)$$

Chemical transport by halide disproportionation reactions has been demonstrated for B, Al, Si, Ge, Ti, Cr, Ga, In, Zr.[60-62] The theory of transport reactions was developed by Schaefer and by Mandel and coworkers[63-66].

The preparation of metal, semiconductor, and oxide films by the thermal decomposition of metal–organic compounds has been actively developed during the last few years[67]. The method, which can call upon an enormous range of initial compounds, is best illustrated by the following reactions:

$$[(CH_3)_2CH-CH_2]_3Al \xrightarrow{\sim 250^\circ} Al + 3(CH_3)_2C=CH_2 + \frac{3}{2}H_2, \quad (23)$$
$$(C_6H_6)_2Cr \xrightarrow{\sim 350^\circ} Cr + 2C_6H_6, \quad (24)$$
$$(C_2H_5O)_4Si \xrightarrow{\sim 800^\circ} SiO_2 + 4C_2H_4 + 2H_2O. \quad (25)$$

The preparation of thin transparent films, of great importance to the optical industry, has been discussed by Suikovskaya[68]. Transparent films deposited on dense, opaque substrates produce a coloration due to the interference of light. In this way, heterogeneous chemical reactions accompanied by a change in the thickness (and hence in the colour) of a film can be made "visible".

II. THE INTERFERENCE INDICATOR METHOD

1. Indicators of Chemical Reactions

We shall use the Russian term "indikator", derived from the Latin "indicator", which means a pointer [69].

All chemical reactions are accompanied by physical effects: heat absorption or evolution, transport of elementary particles (including electrons), changes in weight, volume, and pressure of the reactants, etc. Explosions also produce light and sound effects.

We can often monitor the progress of a chemical reaction by observing changes in some physical property of the reaction system: this property acts as an indicator of (or a pointer to) the state of the reaction. For example, in potentiometric titrations the measured e.m.f. of the system is the indicator property of the system. In the dissociation of a carbonate in a vacuum the indicator property is the increasing pressure of CO_2, which grows to a constant value corresponding to the establishment of a dynamic equilibrium in the system. The inversion of cane sugar can be followed with a polarimeter by observing the rotation of the plane of polarisation of a beam of light passing through the optically active solution.

Often, however, reactions take place without visible change, and the choice of a physical property as an indicator of the path or of the extent of the reaction becomes difficult. Homogeneous reactions in solutions are of this type. In this case one adds to the reaction mixture special substances (indicators) having a property (such as colour) which can be easily monitored and which is sufficiently sensitive to the extent of the reaction.

In the chemistry of aqueous (including some non-aqueous) solutions the indicators are usually organic or inorganic compounds, capable of detecting the end-point of a titration by a colour change, by the appearance or disappearance of a turbidity, by luminescence, etc., or of giving an indication of the value of some physicochemical property of the system such as pH or redox potential. Indicators are usually added to the solution under study in small amounts [70].

During the last 15–20 years the isotopic (including radioactive) indicator method has become very popular: it is based on the "labelled atom" method proposed by Hevesy and Paneth in 1913. Isotopic indicators are substances in which the isotopic composition is different from the natural isotopic composition. They can therefore be used as tracers to study a wide variety of processes. Both stable and radioactive isotopes of the elements can be used as isotopic tracers, since both types of isotope can easily be detected and quantitatively determined [70].

The isotopic indicator method is extremely sensitive; the specificity of these indicators is so high that they can be used in processes involving mixing, migration, and chemical reaction in the most complex systems, including living organisms. The method has therefore been used in studies of the thermodynamics, kinetics, and mechanism of chemical reactions [71–73].

Of course, any indicator has advantages, disadvantages, and limitations. For example, many organic indicators in aqueous solutions are suitable only for identifying the equivalence point in titrations. Radioactive isotopes with very short half-lives have a very limited field of application as indicators; indicators which emit penetrating radiation are dangerous to life and require elaborate screening arrangements.

2. The Interference Colour of Films

One of the most characteristic physical effects of heterogeneous reactions such as oxidation on the surface of a compact monocrystalline or polycrystalline metal is the formation of iridescence (or "temper" colours). This phenomenon has been described in detail [13–18]; a brief discussion of its essential features is given below.

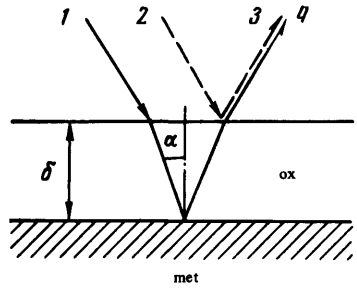


Figure 1. Formation of interference colours in films on metal substrates: *1*) and *2*) incident beams, *3*) and *4*) reflected beams.

When a metal is oxidised by a gaseous reagent (oxygen, chlorine, carbon dioxide, or sulphur, iodine, or water vapour) a transparent, invisible film of product is initially formed on the surface. As the films grows, its thickness becomes comparable with the wave length of visible light, and at this stage interference colours begin to appear.

If a beam of monochromatic light is allowed to strike at right angles the surface of a metal covered by a film, part of the radiant energy is reflected at the film–air interface, and the remainder is refracted into the film and reflected at the metal surface. The condition for destructive interference of the two beams is a phase lag by an odd number of half-waves (Fig. 1); in other words, colours will appear when

$$2\delta = \frac{\lambda}{2n}, \frac{3\lambda}{2n}, \frac{5\lambda}{2n} \ldots \quad (26)$$

where δ is the thickness of the layer of products, λ is the wave length of the light in air, and n is the refractive index of the film.

If a phase change occurs as a result of the double reflection, it can be treated as a correction (c) to the optical path difference:

$$\delta = \frac{\lambda}{4n} - c; \frac{3\lambda}{4n} - c; \frac{5\lambda}{4n} - c \ldots \quad (27)$$

Extinction of part of the visible spectrum by the film produces the complementary colour. As the reaction proceeds, and the film becomes thicker, the colour changes from yellow to blue, as shown by the data on the oxidation of iron [13] given in Table 1.

It follows from the condition for destructive interference that this colour sequence can be repeated as the film continues to grow, giving rise to a second-order spectrum. On some metals it is possible to observe spectra of order three, four, or even five. For example, the book by Bai and coworkers [18] on the oxidation of

titanium and its alloys quotes four distinct interference spectra for oxide films on this metal. Five iridescence spectra were recorded (Table 2) in our continuous observations [74] of the oxidation of titanium in air at 600°†.

Table 1. Interference colours on iron.

Heated in air at 400°		Film thickness, A
time, min	film colour	
1.0	Yellow	460
1.5	Orange	520
2.0	Red	580
2.5	Violet	680
3.0	Blue	720

On titanium, the first-order iridescence spectrum is much more intensely coloured than the higher-order spectra; the spectra of order two, three, and four have pinkish tones, and grey tones are observed at the end of the fifth-order spectrum, indicating a change from interference colours to the genuine colour of the oxide (rutile).

Table 2. Interference colours on titanium heated in air at 600°. (Roman numerals in brackets denote the order of the spectrum.)

Oxidation time	Film colour	Oxidation time	Film colour
0 min 45 s	Dark yellow (I)	63 min 40 s	Crimson
1 min 00 s	Brown	82 min 00 s	Violet
1 min 25 s	Violet	84 min 00 s	Violet-blue
2 min 25 s	Dark blue	88 min 10 s	Green
6 min 30 s	Light blue	113 min	Greenish yellow (IV)
17 min 00 s	Dark yellow (II)	116	Yellowish pink (IV)
22 min 05 s	Crimson	134	Crimson
30 min 00 s	Violet	158	Violet
32 min 30 s	Blue	160	Dark green
38 min 00 s	Dark green	183	Yellowish green (V)
49 min 40 s	Yellow (III)	210	Pink (V)

Because of the development of micro-electronics technology, which relies on thin films of semiconductors and of oxides (insulators), there is a growing awareness of the importance of films showing interference colours. Thin, coloured films on semiconductors such as silicon and germanium are used in practice in structures known as MOS (metal–oxide–semiconductor). [For all practical purposes, MOS technology relies on silicon, not germanium, as the substrate. (Ed. of Translation).]

3. Interference Colour as an Indicator of Heterogeneous Reactions

The colour of thin films on metals and on some semiconductors is a physical effect directly related to a heterogeneous reaction between the solid and its surrounding medium.

The interference colours of thin films have been discussed in depth in the scientific literature. However, most of the published work is concerned with the oxidation of metals by gaseous reagents (see, for example, Refs. 13–18), i.e. with only one type of chemical interaction.

† The temperatures are expressed throughout in degrees Celsius.

Von Wartenberg and Aoyama [75] used the tarnishing of the metal as an indicator in their study of the equilibrium composition of the gas phase in the Cr–O–H system. The interference colour of the oxide film could not be used as a reaction indicator in this work, because it was masked by radiation from the hot metal at the relatively high temperatures used by the authors.

A series of experiments carried out in 1965 by one of us and Agapova [76] demonstrated a reversible colour change when Fe, Ni, and Cu are reduced by hydrogen from their coloured films at relatively low temperatures:

Colour changes during oxidation →

Film colour: yellow brown violet blue

← Colour changes during reduction

That work [76] marked the beginning of a more general use of interference colours as indicators of heterogeneous chemical reactions. It became obvious that interference colours can give valuable information not only on the oxidation of metals, but also on their reduction from the oxides. Reduction reactions can therefore be made "visible", as well as oxidation reactions, by monitoring the colour changes of oxide films in a reducing medium.

Changes in the colour of the films can be seen also during thinning by chemical or electrochemical etching. This information is of fundamental importance in studies of the kinetics and mechanism of the interaction between oxides and electrolyte solutions, and should lead to better control of technological processes for the production of semiconductor and insulator films as well as yielding additional information on the nature of passivating films on metals.

Thus, the change of interference colour during the course of a reaction can be used as an indicator of the extent of reaction in the following systems:

solid–coloured film–gas,
solid–coloured film–liquid,
solid–coloured film–solid.

It is important to remember that a semiconductor, e.g. Si or Ge, can be used in place of the metal, and any other oxidation product, e.g. chloride or bromide, in place of the oxide. Thus, the range of heterogeneous systems in which interference colour can be used as an indicator is very wide indeed.

Several papers in which interference colours are used as indicators of chemical reactions have already been published, and we can therefore state that a new method of physicochemical research has been proposed and validated: the "interference indicator method".

We shall now consider some specific aspects of this method and some concrete results of its application.

III. REACTIONS IN THE METAL–OXIDE–GAS SYSTEM

1. Mechanism

Studies of reactions in the metal–oxide–gas system are very important in clarifying the mechanism of oxidation and reduction reactions of metals: this is particularly true of the theory of heterogeneous chemical reactions in general, and of the theory of metallurgical processes and of the rapidly developing micro-electronics technology in

particular. The use of the interference colours of oxide films as reaction indicators can lead to valuable practical results in these fields of technology.

The generalised equations for the oxidation and the reduction of metals

$$mM_{(s)} + \frac{n}{2}O_{2(g)} \rightleftharpoons M_mO_{n(s)}, \quad (28)$$

$$M_mO_{n(s)} + nB_{(g)} \rightleftharpoons mM_{(s)} + nBO_{(g)}, \quad (29)$$

describe only the quantitative relationships between the reactants, and give no indication whatever of the mechanism of the reaction. The mechanism consists of a series of simple acts and steps, such as diffusion of the reactants in the gas medium and in the layer of products, adsorption and desorption, the chemical act itself, and electron transfer.

The oxidation of metals begins with chemisorption of the oxidising gas, e.g. oxygen, on the metal surface. Oxygen atoms, being electron acceptors, extract electrons from the metal: all the subsequent events on the metal surface stem basically from this cause.

One of the consequences of oxygen chemisorption on a metal surface is the creation of an electric field [15,16] whose value can be as high as 10^7 V cm^{-1}. The electric field can pull cations from the metal lattice into the adsorption layer even at room temperature; its influence was first pointed out by Mott and Cabrera [77,78], whose theory gave the first convincing explanation of the formation of oxide films on metals at low temperatures (i.e. under conditions in which the transport of atoms by diffusion is negligibly small).

Interference colours are observed if a metal is heated after the formation of the primary (low-temperature) oxide film. The theory of Cabrera and Mott, as developed and refined by Wagner, Hauffe, Il'shner, and others [15], can account also for the formation of layers showing interference colours.

Thus, the formation and growth of coloured films is discussed in adequate detail in the theory of the oxidation of metals. However, nothing appears to have been published on the thermodynamics, kinetics, mechanism, and other physicochemical aspects of the reduction of these films to the metal. Some preliminary work in that direction has been done in our laboratory [9,76,79] by observing changes in the interference colours on Fe, Ni, and Cu in a reducing atmosphere.

We found that the reduction of Fe, Ni, and Cu from their coloured films in hydrogen or in carbon monoxide at relatively low temperatures gives colour changes in the opposite sequence to that observed during oxidation. Hence, heterogeneous reactions of the type

$$MO_{(s)} + H_{2(g)} = M_{(s)} + H_2O_{(g)}, \quad (30)$$

$$MO_{(s)} + CO_{(g)} = M_{(s)} + CO_{2(g)}, \quad (31)$$

do not lead to the formation of the product (M) at the oxide–gas interface. Reduction is accompanied by a decrease in film thickness from the direction of the metal substrate.

Our experimental results, combined with the main propositions of the Mott–Cabrera theory, lead to the mechanism shown in Fig. 2 for the reduction of a metal from thin oxide layers. This scheme differs from Richardson and Dancy's [80] in two respects:

1. It emphasises the role of disorder in the oxygen sublattice and of migration of oxygen anions under the influence of the electric field.

2. The disordering of the cation and the anion sublattice, and therefore the generation of the appropriate vacancies, is ascribed to the chemical (reduction) reaction itself.

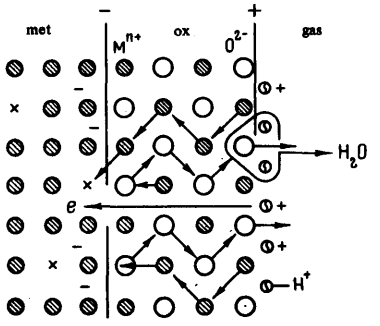


Figure 2. Reduction mechanism of thin metal oxide layers.

The relevance of our experiments, using the colour of the films as a reaction indicator to investigate the mechanism of the reduction of oxide films, is not confined to a reconsideration of the role of oxygen migration in these reactions [81]. The experimental results were used also to identify the site of reactions of the type

$$MO_{(s)} + B_{(g)} = M_{(s)} + BO_{(g)}. \quad (32)$$

Recent publications on the physical chemistry of pyrometallurgical reactions [82,83] attach great importance to the metal–oxide interface, which is assumed to be the reaction surface, i.e. the site of reactions of the type of reaction (32). Once the metal–oxide interface has been formed, reaction (32) is localised at this interface.

Our experimental results on the reduction of coloured oxide films, and the reaction mechanism shown in Fig. 2, are not consistent with the view that the surface-chemical reaction (32) occurs exclusively at the metal–oxide interface. After formation of a metallic phase the reaction is not completely localised at the interface, but it splits up into a series of simpler steps in three-dimensional space, for example:

$$B_{(g)} \rightarrow B^{n+}_{(ads)} + ne_{(ads)}, \quad (33)$$

$$ne_{(ads)} \rightarrow ne_{(m)}, \quad (34)$$

$$M^{n+}_{(ox)} \rightarrow M^{n+}_{(m-ox)}, \quad (35)$$

$$M^{n+}_{(m-ox)} + ne_{(m)} \rightarrow M_{(s)}, \quad (36)$$

$$O^{n-}_{(ox)} \rightarrow O^{n-}_{(ox-g)}, \quad (37)$$

$$O^{n-}_{(ox-g)} \rightarrow O^{n-}_{(ads)}, \quad (38)$$

$$O^{n-}_{(ads)} + B^{n+}_{(ads)} \rightarrow BO_{(ads)}, \quad (39)$$

$$BO_{(ads)} \rightarrow BO_{(g)}, \quad (40)$$

$$MO_{(s)} + B_{(g)} \rightarrow M_{(s)} + BO_{(g)}. \quad (32)$$

The above scheme is justified in our earlier papers [84,85]. Without claiming to be universally applicable, it does illustrate the complexity of the reduction of metal oxides with gaseous reagents, and in particular it shows how spatially separate steps can be combined in the overall mechanism.

One of the theoretical arguments in support of the role of the MO–M interface in surface-chemical reactions of type (32) rests on the application of the law of mass action [82]. We have removed some misconceptions in the application of the law of mass actions to these reactions [86,87].

We have dwelt at length on the mechanism of reactions (28)–(32) because of its relevance to the discussion to follow.

Table 3. Relative increase in the mean rate of oxidation of titanium with increase of temperature during the formation of a first-order coloured film. Mean rate at 500° taken as unity.

Temperature, °C	500	600	700	800
Time for the colour to change over the whole of the first-order spectrum, s	6000	390	70	30
Relative value of the mean rate of oxidation	1	15.4	85.7	200

2. Kinetics

Reaction rates can be inferred from the time for a given change in the colour of the film. For an oxidation reaction we can construct the kinetic curve (film thickness against time) by comparing the colours of films obtained by heating the metal in air or in oxygen for different times with the colours of standard samples.

Tamman [88] described the first experiment of this type. He measured approximate film thicknesses by comparing (in reflected light) the colour of the metal with that of a layer of air between glass plases. The interference colours of a layer of air of variable thickness are given in a table compiled by Rollet. The thickness of the film on the metal was calculated by dividing the thickness of the air gap showing the same colour by the refractive index n of the oxide (or other compound).

Useful kinetic data on the initial stages of oxidation of a metal can be obtained by simple visual observation of colour changes with time, using a stop-clock or a watch. Thus, we have shown [74] that the increase in the mean rate of the initial stage of oxidation of titanium with temperature can be estimated by comparing the times needed to develop the colour corresponding to the completion of the first-order spectrum at different temperatures (Table 3).

A quantitative indication of the retardation of the oxidation of titanium by the increasing thickness of the film of products can be obtained by noting the times needed for the completion of successive spectral orders (Fig. 3).

Depending on the nature of the reactants, on the oxidation temperature, on the range of thicknesses observed, and on other factors, film formation in an oxidising atmosphere is found to obey different kinetic laws (linear, parabolic, or logarithmic) [13–16]. For small changes in thickness (in the range 200–400 Å) the rate of growth is linear to a first approximation, and the mean rate of oxidation is close to the true rate.

Other conditions being equal, the mean rate of oxidation $\bar{V}$ of a metal can be expressed as an exponential function of temperature

$$\bar{V} = \frac{\delta}{\tau} = ke^{-E/RT}, \qquad (41)$$

where δ is the film thickness, τ is time, k is a pre-exponential factor, E is an apparent activation energy, R is the gas constant, and T is the absolute temperature.

For δ = const,

$$\lg\tau = \frac{E}{2.3RT} + C, \qquad (42)$$

and τ and E become the main kinetic parameters of the reaction.

Eqn. (42) suggests a new method of kinetic investigation, which avoids the need for measurements of the film thickness. By choosing a standard interference colour, the time needed to reach a prescribed thickness at different temperatures can be determined visually.

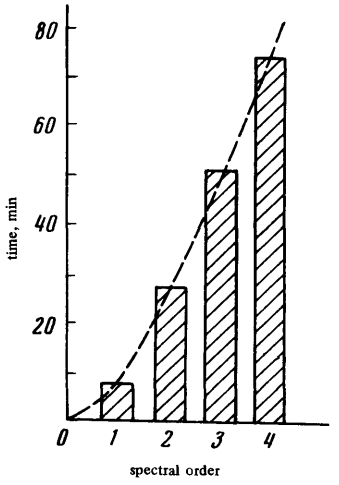


Figure 3. Inhibition of the oxidation of titanium in air at 600° by the increasing thickness of the oxide film.

Using previously published results [9,89], we have made a comparative study of the rates and apparent activation energies for the oxidation of Fe, Ni, and Cu. In the early stages of the reaction, we find that copper oxidises more easily than iron, and the latter more easily than nickel: the colour of the film begins to change appreciably at 200° on copper, at ~300° on iron, and above 400° on nickel.

The interference colour of oxide films has been used also to study the relative rates of oxidation and of Fe, Ni, and Cu [and reduction of their oxides], and also to compare the kinetic efficiencies of two gaseous reducing agents (hydrogen and carbon monoxide) [9,79]. We found that oxidised copper is reduced more easily than oxidised nickel, and the latter more easily than oxidised iron; of the two reducing gases, hydrogen was found to be the more effective.

3. Catalysis

The catalytic effect of the resulting metal on the reduction of an oxide with a gaseous reducing agent is well known: detailed discussions are given in Refs. 90 and 91.

However, the mechanism of the catalytic action is far from perfectly understood. Thus, some workers believe that acceleration of the reaction by the product is possible only when the metal and the oxide are in intimate contact: they assume that the catalytic properties are confined to the metal which is produced by the reaction as a new phase [92]. Other workers [93] report long-range catalytic effects by the product. Further study of these problems is desirable.

Our work with films showing interference colours suggests that it should be possible to observe very much more rapid colour changes in the presence of any agency (such as a catalytically active metal) capable of accelerating the reaction.

As a first step, we examined [10] the catalytic effect of platinum on the reduction of oxidised copper by hydrogen. The catalytic effect of platinum on a wide range of oxidation–reduction reactions is well known [94]. Plates of the electrolytic metal (99.9% Cu), 2 × 1 × 0.2 cm in size, were lapped, polished, and de-greased, and then oxidised in the air at 500° to give a thin, pale-yellow (almost white) film. This interference colour was taken as the standard for the experiment (~950 Å).

The films were then reduced in a hydrogen atmosphere until the interference colour disappeared and the natural colour of copper was restored. The reduction times of the standard film thickness at different temperatures and in the absence of the catalyst are listed in Table 4.

Table 4. Reduction time of a pale yellow film on copper as a function of temperature.

t, °C	200	250	300	350	400	Remark
τ, min	97	25	6	2	0.9	Mean value

The apparent activation energy corresponding to the data of Table 4 is 11.5 kcal mole^{-1}.

The experiment was repeated in the presence of the catalyst, consisting of platinum wires (bright, or coated with platinum black), placed in contact or out of contact with the film surface.

A catalytic effect of platinum on the reduction of oxidised copper was detectable in all the variants of the experiment. The strongest (and most localised) catalytic effect was noted in the experiments in which the wire was platinised and in contact with the sample (Table 5).

The powerful catalytic effect of platinised platinum on the reduction of oxidised copper is evident by simple inspection of Tables 4 and 5. Thus, 97 min were needed to reduce the film at 200° in the absence of the catalyst, whereas the natural colour of copper became visible in less than 7 s in the region adjacent to the contacting surface of Pt black. The acceleration factor for the reduction in the vicinity of the catalyst was 800 or more!

Two observations concerning the action of the platinum catalyst are noteworthy:

1. In the region 40–250° the temperature coefficient of the reaction rate is positive. In the presence of the catalyst the reaction proceeds at a measurable rate even at 40°.

2. At higher temperatures the catalytic activity of the platinum black is substantially lower. Hence, the temperature coefficient of the reaction rate in the presence of the catalyst shows two opposing effects: on the one hand, increase of temperature accelerates the reaction, and on the other hand it lowers the efficiency of the catalyst and thus it inhibits the reaction. We can therefore expect to find an optimum temperature, corresponding to maximum reaction rate. For the range of temperatures of our experiment (40–350°) the optimum is close to 250°.

Table 5. Reduction time of a standard film on Cu in the presence of a freshly platinised wire in contact with the sample.

t, °C	40	50	100	150	200	250	300	350
τ, min	12	3.5	0.75	0.25	0.116	0.0334	0.25	0.33

We have also found [95] that copper has a definite catalytic effect on the reduction of coloured films on copper by carbon monoxide as well as by hydrogen. The largest catalytic effect was obtained with hydrogen, using electrolytic copper as the catalyst.

We have also reported [96,97] a catalytic effect of Pt on the hydrogen reduction of coloured oxide films on Fe. The results are summarised in Table 6.

Table 6. Reduction time of a blue film on iron (to disappearance of colour).

τ, min \ t, °C	250	350	400
Without catalyst	>360	30	3
With catalyst, near contact area	0.333	0.256	0.067

It is evident from Table 6 that the reaction is accelerated by Pt: at 400° the acceleration factor is about 44, at 350° it is 110, and at 250° it is even greater.

In the region close to the platinum contact the reduction proceeds even at temperatures too low to give a significant reaction rate in the absence of the catalyst. Incipient reduction (corresponding to a barely visible colour change) was noted after 10 min at 25°, after 80 s at 50°, and after 35 s at 100°.

Further discussion of the mechanisms of the catalytic action of platinum on the reduction of an oxidised metal, based on observations of changes in the interference colours of the films, can be found in our earlier papers [8,10,97].

IV. REACTIONS IN THE METAL–OXIDE–LIQUID SYSTEM

1. Chemical Etching of Coloured Films on Iron

Uniform dissolution of the films on metals showing interference colours should be accompanied by a sequence of colour changes opposite to the colour changes observed during the growth of the films. This expectation has been confirmed experimentally.

Oxide films often need to be removed from metal articles as the first step in a series of technological operations. Hence, an understanding of the behaviour of films during dissolution has practical as well as theoretical importance.

Experiments with films showing interference colours can be expected to give more reliable results than experiments with thick films, which are liable to contain a greater number of defects such as pores, cracks, bubbles, chemical and structural inhomogeneities.

We believe that all the following questions can be answered by using films showing interference colours to study reactions in the metal–oxide–liquid system:

1. Is a given reagent a suitable etchant for the oxide film on a particular metal? If the etching rate is acceptable, colour changes will be noted in a relatively short time, otherwise the colour will remain unchanged for hours or days.
2. Is the etching action uniform? If the colour changes uniformly, the answer is in the affirmative. Selective etching is indicated by a spotty appearance of the interference colour.
3. Whis is the effect of the nature, concentration, and temperature of the acid?
4. Whis is the effect of convection, ultrasonic irradiation, electric field, etc. on the etching process?

We have used[98] interference colours as a reaction indicator to study the dissolution of oxide films on iron, the commonest of all industrial metals. Polished and de-greased plates of Armco-iron were oxidised in air to a standard interference colour (dark blue) corresponding to a thickness of 720–725 Å.[13] Etching of this film to the disappearance of the interference colour corresponds to a decrease in thickness by about 350 Å, which is of the same order as the thickness of the colourless natural film.

The samples were immersed in solutions of hydrochloric or sulphuric acid, and the colour of the film was continuously noted. The kinetic curves obtained are shown in Fig. 4.

It can be seen that coloured films on iron dissolve at approximately the same rate in hydrochloric and in sulphuric acid over our range of temperatures (20–60°) and concentrations (0.1–1.0 N). Increase of temperature from 20 to 60° increases the rate of the reaction by a factor of 5–6.

For a constant concentration of the etching solution, the etching time is an exponential function of temperature:

$$\tau = Be^{\frac{E}{RT}}, \qquad (43)$$

where B is a constant and E is the apparent activation energy of the dissolution process. The experimental results are satisfactorily described by a linear plot of $\lg\tau$ against $1/T$, which corresponds to the logarithmic form of Eqn. (43):

$$\lg\tau = \lg B + \frac{E}{2.3RT}. \qquad (44)$$

Plots of Eqn. (44) for etching in hydrochloric acid are shown in Fig. 5. The plots for dissolution of the films in sulphuric acid are very similar.

The apparent activation energy E calculated from these plots is 7500–8000 cal mole^{-1}.

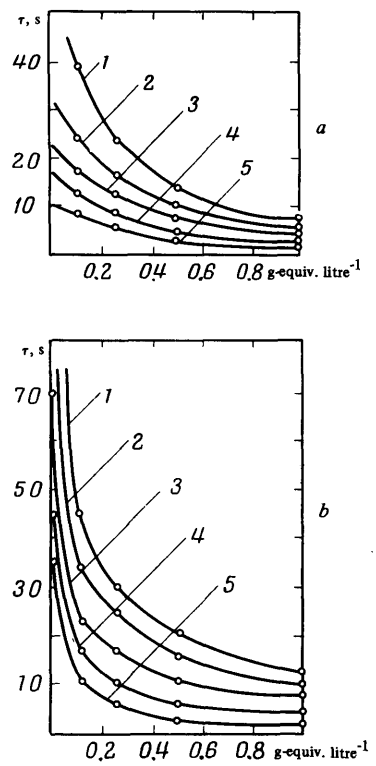


Figure 4. Time for disappearance of interference colour against acid concentration during etching in (*a*) HCl and (*b*) H_2SO_4 at different temperatures: *1*) 20°, *2*) 30°, *3*) 40°, *4*) 50°, *5*) 60°.

2. Behaviour of the Yellow Film on Titanium in Various Inorganic Acid Solutions

The high chemical stability of rutile (TiO_2) towards solutions of inorganic acids has been stressed in the literature[99,100]. Hence it is interesting to study the corrosion behaviour of titanium covered with a thin film of oxide, whose crystal structure is known[18] to be that of rutile.

We have examined the behaviour of titanium samples (OT4-O grade) with a dark yellow oxide film (first-order spectrum) in solutions of HCl, H_2SO_4, HNO_3, H_3PO_4, and CH_3COOH of various concentrations[74]. The samples were immersed in the solutions and monitored visually and gravimetrically.

The behaviour of the interference colours and of the metal in these solutions was somewhat unexpected: as long as a coloured film remained on the metal, the weight of the sample did not change. In these reactions the colour of the film can be used as an accurate indicator of the onset of dissolution.

The beginning of corrosive attack on titanium covered with a yellow oxide film is marked by the appearance of gas bubbles on the metal surface and by the loss of integrity and of uniform coloration of the film: these conclusions are made from visual and gravimetric observations.

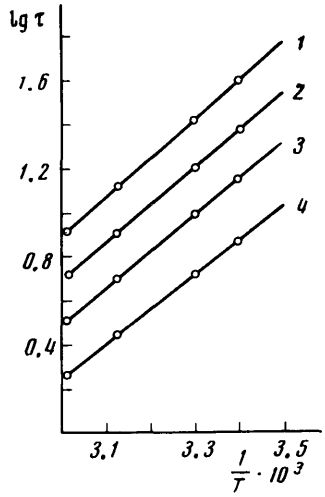


Figure 5. Plots of $\lg\tau = \varphi(1/T)$ for etching in hydrochloric acid solutions of different concentrations: *1*) 0.1 *N*, *2*) 0.25 *N*, *3*) 0.5 *N*, *4*) 1.0 *N*.

The presence of a yellow film on titanium ensures a relatively high corrosion resistance. Thus, in 22% HCl the weight loss of titanium was 2.395 g m^{-2} in 4 h without the yellow film, whereas in the filmed samples the loss was not measurable after 400 h.

In H_2SO_4 solutions of 20–45% concentration the corrosion of samples of the polished metal is slow at first, but it becomes quite fast after an induction period. At 55–96.5% concentrations corrosive attack begins as soon as the sample is immersed in the solution. A peculiar behaviour is observed when Ti is immersed in 75% H_2SO_4: a yellow film is formed on the surface in 20–25 h, and protects the sample for a further 200 h.

The yellow film is highly protective also towards solutions of H_2SO_4. Thus, in 60% H_2SO_4 the loss of unprotected Ti during 4 h is 3.25 g m^{-2}, whereas in the presence of the yellow film the loss is immeasurably small over 320 h.

When samples covered with a yellow interference film are stored in H_2SO_4 solutions of the concentrations used in this work (except 90 and 96.5%) a colour change is observed (Table 7), no doubt due to further oxidation of the metal.

In nitric acid solutions titanium exhibits self-passivation, and hence it is very resistant to corrosion in this medium[99]. Nevertheless, we have detected weight losses with samples of the polished metal in 5–55 wt.% solutions of HNO_3 after 720 h. For example, the loss amounted to 1.026 g m^{-2} in a 25% solution, and to 0.513 g m^{-2} in a 40% solution. In similar experiments with filmed samples, weight losses could be detected only after 1500–1700 h, and amounted to 0.171 and 0.342 g m^{-2} respectively.

Hence, the yellow interference film on titanium offers increased corrosion resistance even in solutions of nitric acid. This conclusion is confirmed by the observation that on storage in HNO_3 solutions of various concentrations the colour of the film changes from yellow towards blue in the same sequence as during the thermal oxidation of titanium to produce films showing a first-order interference spectrum.

Table 7. Colour changes of an oxide film on Ti exposed to H_2SO_4 solutions. (The film was initially yellow.)

Concentration of acid, %	Time of exposure, h	Colour of film after exposure
10	792	Yellow-violet
	960	Violet-blue
	1056	Light blue
25	168	Yellow-violet
	216	Violet-blue
	336	Blue
	480	Light blue
30	144	Yellow-violet
	168	Violet-blue
	216	Blue
	480	Light blue
40	408	Violet-blue
	960	Blue
	1056	Light blue
45	168	Violet
	216	Blue
	240	Light blue

Our experiments with H_3PO_4 showed that in this medium the titanium samples covered with a yellow film are least stable in the concentration range 55–75%, corrosive attack beginning after 365–412 h in these solutions. At concentrations above 75% the corrosion resistance increases appreciably, reaching 892 h in 85% H_3PO_4. Even greater stability, in excess of 1000 h, was found in H_3PO_4 solutions of concentration below 40%.

For comparison, we studied the chemical behaviour of polished titanium (free from interference colours) in H_3PO_4 solutions of the same concentrations. In 35–85% solutions of H_3PO_4 the reaction between the metal and the acid was quite rapid: thus, in a 60% solution the weight loss of titanium in 19 h was 1.539 g m^{-2}. In solutions below 30% concentration the attack on the titanium was very slight at first, and this initial stage was followed by an increase in weight and by the formation of a yellow film, indicating self-passivation of the metal under these conditions.

In acetic acid solutions of 5–45% concentration, titanium covered with a yellow film is extremely stable. Zero weight loss was recorded after 4800 h in acetic acid. On the other hand, samples of polished titanium gave measurable losses after 450–500 h in the same solutions. Thus, oxidised titanium is much more resistant to corrosion than the bright metal even in acetic acid.

The enhanced corrosion resistance of titanium covered with a yellow film, and the mechanism of its corrosion in solutions of HCl, H_2SO_4, and H_3PO_4, may be explained as follows.

During the induction period, when the colour of the film remains unchanged and no gas bubbles are evolved, defects in the film are being slowly eroded. Ultimately the film is punctured at the defective sites, and a "metal–solution" contact is established, leading to the formation of micro-corrosion galvanic couples of the "film–pore" type [13]. Evolution of gas bubbles can then begin, accompanied by disruption of the film, which is lifted from its metallic substrate and loses its protective properties.

V. REACTIONS IN THE METAL–OXIDE–SOLID SYSTEM. CARBO-THERMIC REDUCTION

We have recently extended our study of the possible applications of the "interference indicator method" to reactions between solid phases by investigating the iron–iron oxide–solid carbon system [101,102]. An analysis of this system offers particular interest from the standpoint of metallothermic and carbo-thermic reduction processes.

In order to stress the importance of these results, and the role of interference colours as reaction indicators in this work, we shall dwell briefly on some details of the mechanism of carbothermic reduction reactions, which is discussed in detail in a number of monographs [82,83,103].

In accordance with Baikov's principle of consecutive reactions [82], the final step in the carbo-thermic reduction of iron is usually expressed in the form

$$FeO_{(s)} + C_{(gr.)} = Fe_{(s)} + CO_{(g)}\,. \qquad (45)$$

By combining this equation with the equation for the gasification reaction

$$C_{(gr.)} + CO_{2(g)} = 2CO_{(g)} \qquad (46)$$

we conclude that iron is thermodynamically stable in this system only at temperatures of at least 700°. [82]

Current views on the mechanism of the carbo-thermal reduction of metals from their oxides, depending on the properties of the oxide {stability, volatility [dissociation pressure? (Ed. of Translation)]} and on the experimental conditions (temperature and pressure), are summarised in the following schemes [104]:

Scheme 1
$$MO_{(s)} = M_{(s)} + \tfrac{1}{2}O_{2(g)} \qquad (47)$$
$$\tfrac{1}{2}O_{2(g)} + C_{(gr.)} = CO_{(g)} \qquad (48)$$
$$MO_{(s)} + C_{(gr.)} = M_{(s)} + CO_{(g)} \qquad (49)$$

Scheme 2
$$MO_{(s)} + CO_{(g)} = M_{(s)} + CO_{2(g)} \qquad (50)$$
$$C_{(gr.)} + CO_{2(g)} = 2CO_{(g)} \qquad (51)$$
$$MO_{(s)} + C_{(gr.)} = M_{(s)} + CO_{(g)} \qquad (49)$$

Scheme 3
$$MO_{(s)} = MO_{(g)} \qquad (52)$$
$$MO_{(g)} + C_{(gr.)} = M_{(soln.\ in\ C)} + CO_{(g)} \qquad (53)$$
$$MO_{(s)} + C_{(gr.)} = M_{(soln.\ in\ C)} + CO_{(g)} \qquad (54)$$

All three schemes have one feature in common: gasification of the solid reducing agent. This highlights their common weakness, since it is well known that many different products can be formed when carbon is heated in air: gaseous monoxide and dioxide, and surface oxygen complexes. For example, it has been shown that oxygen becomes chemisorbed on purified carbon at temperatures below 300°, when the formation of gaseous products is negligibly small [105]. Nor should the absorption or occlusion of oxygen by the carbon be ignored.

Thus, there are reasons to suggest that at relatively low temperatures ($t < 500°$) the initial stage of the reaction between metal oxides and carbon does not involve the gasification of the solid reducing agent. But in this case a thermodynamic analysis of the M–O–C system based on Eqn. (45) cannot give a meaningful answer since it does not reflect the real nature of the reaction.

If the reduction gives rise to a metallic phase without the intervention of a gaseous product (CO or CO_2), the process can be tentatively expressed in the form

$$MO_{(s)} + C_{(gr.)} = M_{(s)} + CO_{(s)} \qquad (55)$$

where $CO_{(s)}$ denotes a solid solution of oxygen in graphite, or oxygen chemisorbed on the carbon.

Clearly, the thermodynamic driving force of reaction (55) is not determined by the quantity p_{CO}, but by the activity of oxygen in carbon, in accordance with the reaction isotherm

$$\Delta G = RT\,(\ln a_0' - \ln K_a) \qquad (56)$$

where ΔG is the change in Gibbs free energy of the system attending reaction (55), T is the absolute temperature, a_0' is the non-equilibrium (initial) activity of the oxygen sorbed by the carbon, and K_a is the equilibrium constant of reaction (55): $K_a = a_0$, where a_0 is the equilibrium activity of oxygen.

These considerations raise two important questions:

1. What is the practical importance of reaction (55)?
2. By what method can the reality of reaction (55) be demonstrated?

We shall try to answer both questions.

1. Reaction (55) is undoubtedly vitally important from the viewpoint of the theory of metallurgical processes, but it also has definite practical connotations.

Non-equilibrium structures of the metal–oxide–semiconductor (MOS) type are widely used in modern semiconductor technology. Chemical reactions at the interfacial boundaries of these structures can occur at low temperatures (and, even more so, at high temperatures), and they produce a very undesirable drift in the electrical characteristics of the semiconductor devices made from these structures [2].

In view of the very rapid development of semiconductor technology, the possibility of contact interaction between a conductor (graphite) and a semiconductor (the oxide) is a highly topical problem.

2. Experimental demonstration of the reality of the contact reaction (55) is a very difficult problem, which is the subject of continuing debate (see, for example, Ref. 103).

The very sensitive radioactive indicator method [106], used to detect the temperature at which direct reduction sets in, is inappropriate in this case because it relies on the gasification of "labelled" solid carbon.

We have used the "interference indicator method" to demonstrate the reality of reaction (55). [102] Reduction of a coloured oxide layer should be accompanied by a change in colour, and therefore the chemical interaction should be detectable from the colour change even if the reduction proceeds by the contact mechanism.

A few experiments were made to test this proposition. Samples of Armco-iron were heated in air after being polished and de-greased. When the surface had attained a stable temperature (measured by a Chromel–Alumel thermocouple), and a blue oxide film had appeared, the samples were placed in contact with a pellet of activated charcoal of "Karbolen" grade.

The pellets were pushed aside after various time intervals, and changes in interference colours in the reverse sequence to those corresponding to film growth were observed on the contact surface.

In another series of experiments the pellets were fixed to the specimens with special clamps, and the whole assembly was quenched in water to preserve the colour change. Contact reduction was again observed (see Table 8).

The phenomenon can be observed repeatedly, indicating that the contact reduction is satisfactorily reproducible.

In subsequent experiments by the interference indicator method we observed the contact reduction by carbon of oxide films on Ni at temperatures up to 250°, and on Cu up to 150°.

Table 8. Change of interference colour with time during the contact reduction of oxide films by graphite.

$t = 250°$		$t = 350°$	
Reaction time, s	Film colour	Reaction time, s	Film colour
0	Blue	0	Blue
180	Violet	30	Blue-violet
360	Yellow	60	Brown
630	Colour disappears	90	Yellow

Our results can be interpreted as follows. Oxide films on iron showing the colours of the first-order spectrum consist mainly of the phase α-Fe_2O_3. The temperature at which Fe_2O_3 begins to react with graphite is stated[104] to be 490°, but in our experiments with "interference indicators" chemical reaction between iron oxide and graphite was unmistakably detected at much lower temperature (up to 250°).

All the experiments were carried out in air. It is evident from our results that the presence of an oxidising atmosphere does not inhibit the contact reduction of the oxide film. This may be because the samples had been carefully polished and gave a good contact to the graphite pellet, which also had been polished. Under these conditions the access of air to the contact region was practically excluded.

Low-temperature chemical reactions between solid phases are usually thought to be hindered by the low diffusion rates under these conditions. This view is probably correct for the final stages of a reaction, striving to go to completion, but it cannot be applied to the initial stages. The oxide film on most technical metals (except the noble metals) is formed in the air, at room temperature, in a fraction of a second[6]. The main achievement of the theory of Cabrera and Mott[15] was to provide an explanation of this phenomenon.

In our experiments, too, the contact reaction between solids (oxide and carbon) takes place at an appreciable rate at relatively low temperatures. These results are inexplicable in terms of the standard reaction mechanisms quoted above. They can be explained, however, by the following scheme (Fig. 6). If the contact between the sample and the graphite surface is sufficiently perfect, many points and areas of contact are produced. Carbon, being a reducing agent and therefore an electron donor, can transfer electrons to the metal (an acceptor) through the oxide layer, which is a mixed (electronic–ionic) but predominantly electronic conductor.

This electron transfer generates an electric field across the metal–oxide–graphite system, which produces a kind of electrolysis in the oxide layer: cations migrate towards the metal–oxide interface, and cause the metallic substrate to grow, and oxygen anions migrate towards the graphite, where they are absorbed by the active solid. This process leads to a decrease in thickness of the oxide film, and therefore to a colour change.

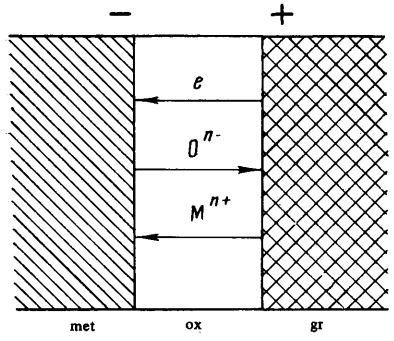


Figure 6. Mechanism of reduction to the metal by contact reaction between an oxide film and graphite.

Thus, by using the interference colour of oxide films on Fe, Ni, and Cu as an indicator of their contact reduction by graphite we have been able to demonstrate a low-temperature chemical reaction between solids and qualify the mechanism of this reaction.

VI. LIMITATIONS, ADVANTAGES, AND DISADVANTAGES OF THE METHOD

It may be concluded from the previous sections that a new method of studying the thermodynamics, kinetics, catalysis, mechanism, and other physicochemical aspects of heterogeneous reactions now exists: the use of the interference colours of thin films as indicators of the extent of reaction. In some cases the colour results from the formation of a thin layer of condensed products, in other cases the coloured layer itself is one of the reactants.

Of course, any method of experimental investigation has a limited region of applications. What are the limitations of interference colour as a reaction indicator?

Firstly (and in contrast to many of the organic indicators used for homogeneous reactions in aqueous solutions) interference colours can be used as indicators of heterogeneous reactions only. The temperature range over which they can be applied extends from room temperature or below to a few hundred degrees: the upper limit of temperature is determined by the stability of the coloured layer itself or by the stability of the underlying substrate.

In principle, the method can be applied whenever a condensed phase is present as a thin film showing interference colours which vary in the course of the reaction.

In this review we have relied mainly on metal–oxide systems to provide illustrations of the interference indicator method. This is partly because these systems are among the commonest and most easily accessible, and partly because of their extreme importance in industrial processes involving the oxidation and reduction of metals (metallurgy, machine construction, micro-electronics, chemical technology). However, the results obtained so

far justify the belief that the method should be equally applicable to systems in which the metal is replaced by a semiconductor and the oxygen by any other non-metal (e.g. S, Se, Te, F, Cl, Br, I). It is well known [3,14] that interference colours can appear on semiconductors as well as on metals, and that many gaseous or liquid reagents can be used instead of oxygen as the film-forming agent.

In summary, the interference indicator method can be recommended for the following specific investigations:

1. Comparing the rates of the initial stage of oxidation of a metal, semiconductor, or alloy at different temperatures with a single oxidising agent, or at a given temperature with different oxidising agents, and also the initial rates of oxidation of different metals and alloys with a given oxidising agent and at a fixed temperature.

2. Determining the rates of reduction of various oxidised metals, and comparing them under different sets of conditions. Quantifying the reducing power of various reagents, i.e. comparing their effectiveness.

3. Studies of heterogeneous catalysis, and comparing the effectiveness of different catalysts.

4. Studies of the solubility of oxides, sulphides, halides, and other compounds which can be prepared as interference-coloured films, in different solvents. Characterisation of the dissolution process, and of its dependence on the nature of the solvent, on temperature, convection, ultra-sonic irradiation, and electric field. In particular, we could study the dissolution of oxygen in a metal, a problem of fundamental importance in the theory and practice of welding, since oxide films are invariably present on the surface of metals being welded.

5. Studies of electrochemical processes in the metal–oxide–electrolyte system, and further investigation of the nature of metal passivity.

6. The contact interaction of solid phases, a problem of over-riding urgency in the rapidly developing technology of micro-electronic devices. The method seems particularly adapted to the very systems of interest in micro-electronics.

The range of applications of the method is not, of course, limited to the above recommendations, and is likely to be further extended by the results of future work.

We shall now discuss the advantages and disadvantages of interference colour as an indicator of chemical reactions.

In the present review, certain aspects of the method have been specially stressed in order to demonstrate its simplicity and attractiveness. It requires no specialised or dedicated equipment, such as is used in the isotopic and radioactive indicator methods. In most cases the experiment can be easily arranged for convenient observation of the colour of the film. The temperature and pressure regions over which the method can be applied are sufficiently wide.

The method is entirely free from hazards, and does not require the special safety precautions and apparatus screening arrangements inherent in the use of radioactive indicators.

The main shortcoming of interference indicators is the fact that coloured films cannot be obtained in all systems. The method is not suitable for heterogeneous reactions in which the condensed phase is in a finely divided state.

Of course, any experimental method must have some weaknesses. However, new procedures should always be welcomed because they offer new possibilities to the experimenter. The present review aims to bring to the attention of its readers a new and (we believe) powerful method of studying heterogeneous reactions.

In conclusion, we offer some additional comments on the concept of a reaction indicator. The use of interference colour as an indicator of heterogeneous chemical reactions is an extension of the concept, and gives a new slant to the theory of chemical reaction indicators.

In contrast to homogeneous reactions in solutions, for which whole systems of special indicators have been developed, heterogeneous reactions have lacked special indicators of the extent of reaction. In some systems, stable or radioactive isotopes have been used as heterogeneous reaction indicators, but their complexity, limitations, and practical disadvantages are well known, and are mentioned in this review.

Our experiments with various interference indicators of heterogeneous reactions have shown that, as in the case of homogeneous reactions in aqueous solutions, the indicator produces a definite colour in the medium, varying with the extent of reaction or at a predetermined stage in the reaction. This clear analogy justifies the use of interference colour as a chemical reaction indicator, and we propose the term "interference indicator method" for the use of interference colours in this context.

As commonly used, the term indicator denotes a substance specially added to the reaction system to make visible the progress of the reaction. The increasing use of interference colours and of other criteria and properties of the reactants as indicators in heterogeneous reactions creates a need to reconsider and to extend the concept and the definition of a chemical indicator [2].

We propose the following comprehensive definition: a chemical reaction indicator is any easily observed criterion or property of the reaction system, or of the reactants, which changes during the course of the reaction, thus allowing the course of the reaction and its extent to be monitored. The property may be inherent in one of the reacting phases, or it may be contributed by a specially added substance.

In accordance with this definition, all indicators can be divided into two classes.

1. Intrinsic indicators. These include the criteria and properties which are fundamental to the reaction system or to the reactants. If they are easily observable, and if they change during the reaction, they allow the course of the reaction to be monitored: for example, changes in weight, volume, or pressure of the reactants. Other indicators belonging to this class are the varying e.m.f. of the system during a potentiometric titration, and the angle of rotation of plane polarised light during the inversion of cane sugar. Films showing interference colours can also be classified as intrinsic indicators.

2. Impurity indicators. These include all organic and inorganic substances added to reaction mixtures to produce a colour, luminescence, or other physical property varying during the reaction. Isotopic indicators belong to this class.

Alternatively, indicators could be classified according to the type of chemical reaction as *homogeneous* or *heterogeneous*.

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Voronezh Polytechnic
Institute, Physical
Chemistry Department

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Vibrations of the Ethynyl Group (C≡C-H), the Hydrogen Bond, and Intramolecular Interactions in Monosubstituted Acetylenes

E.A.Gastilovich and D.N.Shigorin

The problem of whether or not the vibrations of the ethynyl group are characteristic has been examined and data are presented for the vibration modes, the potential fields, and the electro-optical parameters. Much attention has been devoted to the spectroscopic model of the hydrogen bond. Various methods of investigating intramolecular interactions in acetylene derivatives (containing halogen, Si, Sn, and N atoms as well as groups with π-electrons) by vibrational (infrared) spectroscopy have been considered.
The bibliography includes 94 references.

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I. INTRODUCTION

Acetylene and its derivatives are extensively used to synthesise a wide variety of compounds employed in industry. The physical and chemical properties of compounds of the acetylene series are largely determined (owing to the characteristics of the electronic structure of the C≡CH group) by intramolecular and intermolecular electronic interactions. The changes in the electronic structure of the molecules are clearly reflected in the vibration spectra. At the end of the 1950's and in the 1960's, there was an appreciable increase of interest by

spectroscopists in the study of acetylenic compounds. The simple linear structure of the ethynyl groups $-C\equiv C-H$ provided a convenient model for the investigation of the nature of the hydrogen bond and its manifestations, a problem which has been discussed for a long time. On the other hand, in order to create new polymers, new derivatives of acetylene containing various heteroatoms, particularly those of elements of Group VI and others, were synthesised. It was necessary to investigate the intramolecular interactions of these compounds of these compounds. However, the application of vibration spectroscopy to the study of electronic interactions in molecules is impossible without the knowledge of the spectroscopic characteristics of the vibrations considered. At present there is no complete review in the literature devoted to closely related problems such as the characteristics of the vibrations of the ethynyl group and the manifestation of intramolecular and intermolecular interactions in the vibration spectra of acetylene derivatives. Therefore we hope that the present review will be of interest to specialists working in the field of the chemistry and spectroscopy of acetylene and its derivatives.

II. VIBRATIONS OF THE ETHYNYL GROUP

The principle data on the vibration frequencies of the ethynyl group $C\equiv C-H$ have been presented, for example, in Bellamy's monograph [1], which contains information about the influence of various substituents in the molecule on the vibration frequencies of this group. Luneva's review [2] is devoted to acetylene derivatives containing Group IV elements, but it gives little space to spectroscopic studies on these compounds. We may note that the study of intramolecular interactions by infrared absorption (i.r) and Raman spectroscopy must be based on the knowledge whether or not the vibrations of a particular group of atoms are characteristic as regards frequency, mode, and intensity. When these vibrational characteristics are ignored, those conclusions concerning the mutual influence of individual groups of atoms in the molecule which are based only on experimental vibration frequencies and intensities of the corresponding bands and lines in infrared and Raman spectra become baseless.

1. Vibration Mode and Frequency

The stretching vibration frequencies of the $C\equiv C$ and $\equiv CH$ groups in acetylenic compounds ($\nu C\equiv C$ and $\nu\equiv CH$) occur in a part of the spectrum which is free from the vibrations of most other polyatomic molecular groups (2250–1950 cm^{-1} and 3300 cm^{-1} respectively).

In the simplest example of compounds of this class, i.e. acetylene ($HC\equiv CH$), the sharp change in the vibration frequency of the $C\equiv C$ group following the substitution of the hydrogen atom by deuterium is associated with the mechanics of the vibrations [3]. The problem of whether or not the vibrations of the ethynyl group show characteristic frequencies and modes in acetylene derivatives of different structures has been considered by Gastilovich, Shigorin, and coworkers [4–8], Popov and coworkers [9–11], Duncan [12], and Zerbi and Gussoni [13].

Calculations on the vibrations in acetylene derivatives such as methylacetylene, t-butylacetylene, trimethylsilylacetylene, and halogenoacetylenes led to the conclusion that the $\nu C\equiv C$ vibration mode is not determined by the $C\equiv C$ group alone [4,12]. Having considered the $\nu C\equiv C$ and $\nu\equiv CH$ stretching vibrations in monoalkyl-, monosilyl-, monostannyl- and monovinyl-acetylenes, the present authors and their coworkers [4–8] concluded that the modes of these vibrations do not change and are characteristic for the $\nu C\equiv C$ vibrations of the entire $X-C\equiv C-H$ group and for the $\nu\equiv CH$ vibrations of the $C\equiv C-H$ group. Data concerning the mode of the stretching vibrations of the $X-C\equiv CH$ group in molecules with a very wide variety of structures—alkyl-, vinyl-, and phenyl-derivatives as well as derivatives containing Group IV atoms in the α-positions —are presented in Table 1†. The data in Table 1 show that the $\nu\equiv CH$ and $\nu C\equiv C$ vibrations are localised in the $X-C\equiv C-H$ group and their mode remains unchanged. An exception is the $\nu C\equiv C$ vibration in methylacetylene according to the data of Lubuzh and Popov, whose calculations showed that the C–H bonds of the methyl group are involved in this vibration [9]. Duncan's calculation for the same molecule, according to which the $\nu C\equiv C$ vibration is localised at the $C-C\equiv C-H$ group, is inconsistent with this conclusion [12].

Table 1. Modes of the stretching vibrations of the $X-C\equiv C-H$ group in certain monosubstituted acetylenes.

Compound	Vibration frequency ν, cm^{-1} (expt.)	Vibration modes: q	Q	Q_1	Q_2	β	explanation	References
$CH_3C\equiv CH$	$\nu_{\equiv CH}$ 3334	1.00	−0.13	0.03			Q_2(C–H) $\beta(\angle HCC\equiv)$	9
	$\nu_{C\equiv C}$ 2142	0.11	0.34	−0.17	−0.35	−0.12		
	$\nu_{\equiv C-Q}$ 931	0.03	0.06	0.29	0.01	−0.04		
$CH_3C\equiv CH$	$\nu_{\equiv CH}$ 3334	1.03	−0.13	0.03	0	0	Q_2(C–H) $\beta(\angle HCC\equiv)$	12
	$\nu_{C\equiv C}$ 2142	0.14	0.38	−0.25	−0.02	−0.02		
	$\nu_{\equiv C-C}$ 931	0.01	0.06	0.28	0.02	−0.10		
$R_3X-C\equiv CH$, X=C, Si $R_3=(CH_3)_3$; X=Sn $R_3=(C_2H_5)_3$	$\nu_{\equiv CH}$ C 3312	0.99	−0.13	0.03	—	—	Q_2(C–X) $\beta(\angle XCC\equiv)$	5,14
	Si 3292	0.99	−0.13	0.03	—	—		
	Sn 3287	0.99	−0.13	0.03	—	—		
	$\nu_{C\equiv C}$ C 2103	0.13	0.38	−0.25	—	—		
	Si 2035	0.12	0.38	−0.22	—	—		
	Sn 2005	0.12	0.39	−0.21	—	—		
	$\nu_{\equiv C-X}$ C 693		0.02	0.13	0.11	0.03		
	Si 556		0.02	0.19	0.09	−0.02		
	Sn 425		0.02	0.20	0.02	−0.01		
	$\nu_{\equiv CH}$ 3326	1.00	−0.13	0.03			Q_2(C=O) $\beta(\angle OCH)$ $\beta(\angle \bar{O}CC\equiv)$	11
	$\nu_{C\equiv C}$ 2106	0.12	0.38	−0.29	0.05	−0.10		
	$\nu_{\equiv C-C}$ 944	0.01	0.06	0.27	0.03	−0.23		
R'YCH= =CH–C≡ ≡C–H Y=N, S, O	$\nu_{\equiv CH}$ 3310–3315	0.99	−0.12	0.03	—	—	Q_2(C=C) $\beta(\angle HCC\equiv)$ $\beta(\angle HCC\equiv)$	15
	$\nu_{C\equiv C}$ 2075–2100	0.13	+0.38	−0.27	0.05	0.08		
	$\nu_{\equiv C-C}$ 930–960	0.01	0.05	0.24	0	−0.20		
	$\nu_{\equiv CH}$ 3315	0.99	−0.13	0.03	—	—	Q_2(C=C)arom 	16
	$\nu_{C\equiv C}$ 2119	0.13	0.37	−0.27	0.03	−0.07		
	$\nu_{C-C\equiv}$ 1192	0.01	0.05	0.22	−0.08	0.22		

The knowledge of the vibration mode is necessary to decide whether or not the vibrations have characteristic intensities. On the other hand, the knowledge of the modes of the $\nu\equiv CH$ and the $\nu C\equiv C$ vibrations makes it

†The vibration modes have been recalculated in terms of a single system of units (see text); the designations of the coordinates are indicated in the Figure.

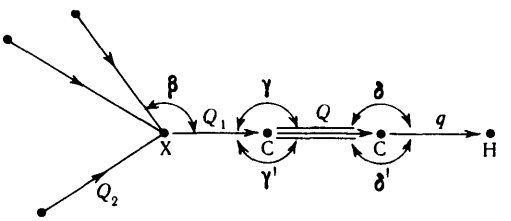
possible to calculate the dependence of these vibration frequencies on the changes of the dynamic (force) constants of the X—C≡C—H group. Thus the familiar expression for the derivative of the square root of the vibration frequencies with respect to the force constant K as a function of the vibration mode [17] yields the following relations:

$$\begin{array}{c|c|c} \Delta K_q = +1.0 & \Delta H_q^Q = +1.0 & \Delta H_{Q_1}^Q = +1.0 \\ \Delta\nu_{\equiv CH} = +136\ cm^{-1} & \Delta\nu_{\equiv CH} = -32\ cm^{-1} & \Delta\nu_{\equiv CH} = +2\ cm^{-1}; \end{array} \quad (1)$$

for the ≡C—H group ($\nu_{\equiv CH}$ = 3310 cm^{-1}) and

$$\begin{array}{c|c|c} \Delta K_Q = +1.0 & \Delta K_{Q_1} = +1.0 & \Delta H_{Q_1}^Q = +1.0 \\ \Delta\nu_{C\equiv C} = +34\ cm^{-1} & \Delta\nu_{C\equiv C} = +14\ cm^{-1} & \Delta\nu_{C\equiv C} = -43\ cm^{-1} \\ \Delta K_q = +1.0 & \Delta H_q^Q = +1.0 & \\ \Delta\nu_{C\equiv C} = +3\ cm^{-1} & \Delta\nu_{C\equiv C} = +22\ cm^{-1} & \end{array} \quad (2)$$

for the C≡C group (νC≡C = 2100 cm^{-1}). The generally accepted notation for force constants is employed here [17] (in units of 10^6 cm^{-2}). The designations of the normal coordinates are shown in the Figure. The relations show clearly the characteristic nature of the $\nu_{\equiv CH}$ and νC≡C vibrations as regards frequency. On the other hand, they make it possible to explain the differences between the force constants calculated by a different investigators from the experimental vibration frequencies of the same molecule.



Designation of the natural coordinates.

Certain dynamic constants of the X—C≡CH group in molecules of different structures, calculated by different investigators, are listed in Table 2. In the studies under consideration, the dynamic constants were expressed in different units. In Table 2 and throughout the text, all the constants are given in units of 10^6 cm^{-2}; 1 Å and one atomic mass unit (1/16 of the mass of the oxygen atom) being adopted as unit length and unit mass respectively.

The $\nu_{\equiv CH}$ vibration frequency is determined by only two constants: K_q and to some extent H_q^Q. Table 2 shows [5,9,12,14] that the large differences between the K_q in various studies can be accounted for by the fact that some investigators introduced the spectroscopic mass of the hydrogen atom (1.088 a.m.u.) when $K_q \simeq 10.88$–10.55 cm^{-2} while others assume that the mass of the hydrogen atom is 1.008 a.m.u. ($K_q \simeq 10.1$–9.83) (in this case the conversion factor for K_q is approximately 1.07. The coefficient H_q^Q plays a relatively small role and probably cannot be determined reliably from vibration frequencies in infrared spectra. Thus significantly different H_q^Q values are quoted by Duncan [12], by Popov and Gribov [19], and by Lubuzh and Popov [9] for almost the same set of molecules (Table 2 does not list all the data).

The νC≡C vibration is characteristic as regards mode and frequency for the X—C≡C—H group. Table 2 shows that the constants K_Q, K_{Q_1}, H_q^Q, and $H_{Q_1}^Q$ which determines the frequency of this vibration, are extremely different for the same or similar compounds (Table 2) [6,10,12,13,16]. Firstly, this difference is due to the fact that the νC≡C vibration frequencies were calculated by the authors with different accuracies ($\nu_{C\equiv C}^{exp} - \nu_{C\equiv C}^{calc}$). Secondly, since the vibration frequency depends to an almost equal extent on the four force constants, the uniqueness of this set of constants depends on the accuracy of the calculation for other vibrations too ($\nu_{\equiv C\text{-}X}$, ν_p). Otherwise the set of constants K_Q, K_{Q_1}, H_q^Q, and $H_{Q_1}^Q$ becomes arbitrary (Table 2) [6,10,16]. The variation of their values in each set obeys Eqns. (2). The sets quoted by Lubuzh and Popov for methylacetylene and by Zerbi and Gussoni [13] for the compounds H_2XC—C≡CH constitute an exception. This is probably because the νC≡C vibration mode differs from that used in the remaining calculations. We noted above that this was the case in Lubuzh and Popov's study [9]. In contrast to the remaining investigations, Zerbi and Gussoni [13] employed a potential field of a mixed type: a valence force field for the C≡C—H group and a Urey–Bradley field for the H_2XC-group, which probably affected the vibration mode (data for the mode are not quoted).

The absorption bands for the deformation vibrations of the ≡C—H group lie in the range 610–680 cm^{-1}. [1] The stretching and deformation vibration in the ethynyl group are fully separated [19]. According to the data of Duncan [12], Lubuzh and Popov [9], Epshtein and Popov [11] and others, the amplitudes of the changes in the angles δ and γ (see Figure) in the δ≡CH vibration differ by a power of ten. From the form of this vibration mode, it is possible to obtain relations between the changes in the dynamic constants for the —C≡C—H group and the changes in the δ≡CH vibration analogous to Eqns. (1) and (2):

$$\begin{array}{c} \Delta K_\delta = \pm 0.1\ (\times 10^6\ cm^{-2})\ \ \Delta K_\gamma = \pm 0.1\ \ \Delta l_\gamma^\delta = \pm 0.1 \\ \Delta\delta_{\equiv CH} = \pm 90\ cm^{-1}\ \ \Delta\delta_{\equiv CH} = \pm 1\ \ \Delta\delta_{\equiv CH} = -18 \end{array} \quad (3)$$

The δ≡CH vibration in acetylene is doubly degenerate. In monosubstituted acetylenes, this degeneracy is removed and two bands ($\delta_{\equiv CH}^{(1)}$ and $\delta_{\equiv CH}^{(2)}$) are observed in the spectrum. The different possible mechanisms of the intramolecular interactions, which leads to a splitting of the δ≡CH band, have been considered by Nyquist and Potts [23]. The splitting can reach several units. Thus, in vinylacetylenes with a heteroatom Y = S, O, or N in the —RYCH=CH—C≡CH conjugated chain, $\delta_{\equiv CH}^{\perp} - \delta_{\equiv CH}^{\parallel} = 48$, 50 and 107 cm^{-1} respectively [15], which corresponds to a change in $K_\delta^\perp - K_\delta^\parallel$ of about $(0.05$–$0.12) \times 10^6$ cm^{-1}. This is a considerable difference bearing in mind that the force constant K_δ is itself small ($K_\delta = 0.375 \times 10^6$ cm^{-2}, $\delta_{\equiv CH}$ = 633 cm^{-1}) [9].

2. Electro-optical Characteristics from Infrared Spectra

The problem of whether or not the vibrations of the ethynyl group show characteristic intensities can be treated on the basis of the valence-optical theory of intensity [24]. As a result of its development by Gribov, a computational scheme was put forward where the electro-optical parameters (EP) μ_i, $\partial\mu_i/\partial q_i$, and $\partial\mu_i/\partial\alpha_j$ (μ_i is the dipole moment of the ith bond and q and α are the normal coordinates of the bond and angle) were introduced as the

Table 2. The force constants K (in units of 10^6 cm^{-2}) and the calculated and experimental frequencies ν (cm^{-1}) of the stretching vibrations of the X—C≡CH group in certain acetylene derivatives.

Compound	K_q	K_Q	K_{Q_1}	H_q^Q	$H_{Q_1}^Q$	calc $\nu_{\equiv CH}$	exp $\nu_{\equiv CH}$	calc $\nu_{C\equiv C}$	exp $\nu_{C\equiv C}$	calc $\nu_{\equiv C-X}$	exp $\nu_{\equiv C-X}$	Refs.
$H_3FC-C\equiv CH$	10.1	23.91	12.1	0	0	3335	3338	2149	2150	939	940	
$H_3ClC-C\equiv CH$	10.1	23.91	12.2	0	0	3335	3335	2137	2147	962	960	
$H_3BrC-C\equiv CH$	10.1	33.91	12.3	0	0	3335	3335	2137	2138	962	961	13
$H_3IC-C\equiv CH$	10.1	23.91	12.55	0	0	3335	3335	2142	3130	952	959	
$ClC\equiv CH$	10.15	26.8	9.15	0	0	3372	3340	2122	2110	759	756	
(D)						(2627)	(2612)	(1987)	(1980)	(742)	(742)	18
$CH_3-C\equiv CH$	10.1	26.9	9.00	0	0.31	3346	3334	2151	2141	929	931	
(D)						(2607)	(2617)	(2005)	(2008)	(916)	(—)	
$H_3C-C\equiv C-CH_3$	—	26.6	8.95	—	1.03	—	—	2240	2240	725	725	12
										1152	1152	
$H-C\equiv CH$	10.1	26.7	—	0.05	—	—	—	—	—	—	—	
$Cl-C\equiv CH$	10.15	26.3	9.05	0	0.51	3351	3340	2114	2110	756	755	
$HC\equiv CH$	10.70	26.8	—	0.22	—	3278	3287					
(D)						(3317)	(3335)	(1856)	(1851)	(2573)	(2585)	19
$DC\equiv DC$						2437	2428					
$H_3C-C\equiv CH$	10.88	26.6	8.7	0.22	0.11	3339	3334	2146	2142	914	931	
$F-C\equiv CH$	10.88	28.3	13.7	0.22	1.09	3358	3355	2230	2245	1059	1055	
$Cl-C\equiv CH$	10.88	26.1	9.35	0.22	0.54	3336	3340	2111	2110	742	756	9
$Br-C\equiv CH$	10.80	25.5	7.8	0.22	0.32	3328	3325	2077	2085	616	618	
$IC\equiv CH$	10.70	25.3	7.6	0.22	0.21	3324	3320	2073	2075	590	~600	
O ‖ C—C≡CH / H	10.77	24.6	10.9	0.22	0.22	3324	3326	2110	2106	938	944	11
$H_3C-O-C\equiv CH$	10.88	26.3	13.6	0.21	0.762	3338	3361 3352 3345	2182	2182 2171 2161	930[s] 1195[as]	943—895[s] 1221—1201[as]	20
$(CH_3)_3-C-C\equiv CH$	9.90	26.00	8.8	0.05	0.50	3303	3309	2122	2120	1060	930	
(D)						(2577)	(2593)	(1985)	(1971)			4,
$(CH_3)_3SiC\equiv CH$	9.83	25.2	5.90	0	0.25	3289	3292	2042	2035	554	556	5
(D)						(2552)	(2572)	(1913)	(1909)			
$(C_2H_5)_3Sn-C\equiv CH$	10.50	25.0	4.1	0	0.23	3286	3287	2009	2005	425	425	
(D)						(2566)	2560	1882	1879			14
$(C_2H_5)_2Sn(C\equiv CH)_2$	10.52	25.2	4.1	0	0.23	3290	3293	2017	2017	416[s]	420	
										439[as]	434	21
$C_2H_5-Sn(C\equiv CH)_3$	10.55	25.43	4.1	0	0.23	3295	3296	2026	2034	396[s]	—	
										444[as]	443	
$H_2C=HC-C\equiv CH$	10.88	24.2	12.0	0.22	0.54	3334	3335	2095	2099	920	929	
$H_2C=CH-C\equiv C-CH_3$	10.88	24.2	12.0	0.22	0.54	—	—	2227	2235	927	920	10
$H_2C=C(CH_3)C\equiv CH$								2098	2100	931	952	
$RHC=HC-C\equiv CH$	9.95	26.0	8.8	0.05	0.50	3310	3314	2113	2100	965	930—960	6
	10.6	26.0	8.3	0	0	3305	3315	2124	2119	1215	1192	
						(2628)	(2608)	(2002)	(1989)	(1210)	(1189)	16
$H-C\equiv C-C\equiv C-H$	10.70	24.1	12.8	0.22	0.54	3333	3329	2011	2020			
					−1.63*							22
$CH_3C\equiv C-C\equiv C-CH_3$						—	—	2166	2163	930	941	

* $H_Q^{Q'}$.

characteristics of the bonds and angles in the molecule[25]. Adopting further reasonable approximations (the zeroth approximation when only the diagonal elements are non-zero as well as higher degrees of approximation), it is possible to assess from the electro-optical parameters (and not from the intensities of the infrared absorption bands) for molecules of similar structures the mutual influence of the individual groups of atoms in the molecule. This treatment is analogous to the consideration of force constants instead of vibration frequencies in the study of the effect of intramolecular interactions on vibration frequencies.

The electro-optical parameters for acetylene[19,26], t-butylacetylene[5], vinylacetylene and diacetylene[27], trimethylsilylacetylene[5], and organotin derivatives of acetylene with several ethynyl groups[14,21] have now been

calculated from experimental intensities of infrared absorption bands and are listed in Table 3. Popov et al.[27] also determined the dipole moments of the C≡C bonds ($|\mu_Q| = 1.0$ D) for diacetylene and vinylacetylene and the C=C bond ($|\mu_{Q_2}| = 0.70$ D) for the latter.

Table 3. The electro-optical parameters $\partial\mu_i/\partial q_i$ [D/Å] and μ[D] of the CXC≡CH groups and the experimental absolute intensities B (in units of 10^4 cm^{-2} litre mole^{-1}) of the absorption bands associated with the C≡C—H groups in the infrared spectra.

Chemical formula	Electro-optical parameters					Intensity		References
	$\lvert\mu_q\rvert$	$\frac{\partial\mu_q}{\partial q}$	$\frac{\partial\mu_Q}{\partial Q}$	$\frac{\partial\mu_{Q_1}}{\partial Q_1}$	$\frac{\partial\mu_{Q_2}}{\partial Q_2}$	$B_{\nu C\equiv CH}$	$B_{\nu C\equiv C}$	
HC≡CH	0.94	0.826[a]					inactive	26
H—C≡CH	1.1	0.90					inactive	19
H_2C=CH—C≡CH	0.90	1.0	0.10	−0.35	1.0	0.41	0.004	27
HC≡C—C≡CH	0.80	0.90	−0.10[b]			0.61	0.013	27
$(CH_3)_3C$—C≡CH	1.24	1.22	−0.75[a]	0.90	—	0.73	0.063	5
$(CH_3)_3Si$—C≡CH	1.12	0.97	−1.02	−4.6	2.0	0.46	0.25	5
$(C_2H_5)_3Sn$—C≡CH	1.30	0.85	−1.85	−5.2	2.4	0.45	0.10	14
$(C_2H_5)_{4-n}Sn(C\equiv CH)_n$		0.85	−1.85	−5.2		0.89(n=2)	0.31(n=2)	21
				+1.2[c]	2.5	1.20(n=3)	0.63(n=3)	

Note. The values listed in the Table correspond to the following combinations of electro-optical parameters in the publications quoted: [a] $\partial\mu_q/\partial q - \partial\mu_q/\partial q'$; [b] $\partial\mu_Q/\partial Q - \partial\mu_Q/\partial Q'$; [c] for all the R_3X—C≡CH, $\partial\mu_q/\partial Q + \partial\mu_Q/\partial Q + \partial\mu_{Q_1}/\partial Q$; [d] $\partial\mu_{Q_1}/\partial Q_1'$ (the prime indicates an equivalent but "foreign" coordinate).

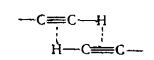
It has been shown[5,7,14] that the ν≡CH vibration in molecules of different structures is characteristic as regards intensity. In other words, the intensity of the corresponding absorption band in the infrared spectrum is determined mainly by the electro-optical parameters for this bond ($\partial\mu_q/\partial q$). On the other hand, the intensity of the νC≡C vibration band is characterised by the set of electro-optical parameters of the entire X—C≡C—H group and $\partial\mu_Q/\partial Q$ does not play a decisive role. Thus, in compounds with a heteroatom (X = Si and Sn), both the direction of the dipole moment of the transition $\partial\vec{M}/\partial Q_{C\equiv C}$ ($\vec{M}$ is the dipole moment of the entire molecule and $Q_{C\equiv C}$ the normal coordinate of the νC≡C vibration) and the intensity of the νC≡C band are determined by the parameters of the X—C≡ bond and not the C≡C bond. A similar phenomenon has been observed for another class of compounds—ethylene derivatives, for which it has been shown that the intensity of the C=C absorption band ($\nu_{C=C}$) is not determined by the parameters of this bond[28]. The low contribution of the electro-optical parameters of carbon chains to the intensity of the absorption bands associated with the skeletal vibrations of the molecule was noted previously by Gribov and Popov[29]. Thus theoretical calculation of the absorption band intensities in the infrared spectrum of dimethylacetylene using only the electro-optical parameters of the C—H bonds in the ethane molecule[30] gave satisfactory agreement between the calculated and experimental values for all these vibrations. Hence it was found that the electro-optical parameters of the C—C≡C—C group in the dimethylacetylene molecule may be neglected. However, in the vinylacetylene and diacetylene molecules[27] as well as in other monosubstituted acetylenes (Table 3), the electro-optical parameters of the multiple bonds are fairly large.

In a study of the intensities of the νC≡C absorption bands in the spectra of compounds with a complex molecular structure, RYCH=CH—C≡CH and RYCH=CH—C≡C—Si$(CH_3)_3$ (R = alkyl; Y = S, O, or N atom), Gastilovich, Shigorin et al. concluded that the νC≡C intensity depends on the electro-optical parameters of the Y—C= group[7,15]. They also concluded that in molecules with conjugated bonds and with a heteroatom, the νC≡C vibration remains characteristic as regards frequency and mode for the C—C≡C—H group but cease to be characteristic as regards intensity for this group. The νC≡C intensity is determined by the electro-optical parameters of the entire YCH=CH—C≡CH group; this corresponds, within the framework of the valence-optical theory of intensity, to the employment of high degrees of approximation, which is probably impossible in practice.

The results of studies on intermolecular interaction (the hydrogen bond in acetylene derivatives), such as the electron-donating and electron-accepting properties of the —C≡C—H group and changes in the absorption band intensities in electron-donating solvents, can also be very useful for the solution of the problem of intramolecular interactions. Therefore, having considered the problem of whether or not the vibrations are characteristic, we proceed to the problem of the hydrogen bond in acetylene derivatives.

III. THE HYDROGEN BOND

As early as 1939, the anomalously high solubility of acetylene in electron-donating solvents (EDS) and the experimental heats of solution in such solvents led Copley and Holley to the conclusion that there is a specific intermolecular interaction in such solutions between the acetylene and solvent molecules[31]. In 1941 Standford and Gordy observed in the infrared spectra of phenylacetylene solutions in EDS a bathochromic shift of the absorption band due to the stretching vibration of the ≡C—H group. The shift was of the same order of magnitude as that observed for the OD group in deuteriated alcohols. The authors concluded that a hydrogen bond is formed in phenylacetylene solution in EDS.[32] In 1958, Shigorin and coworkers suggested, on the basis of a study of the spectra of vapours and liquids, the formation of a specific hydrogen bond between the molecules of acetylene derivatives involving the π-electrons of the C≡C group (electron-donating group) and the orbitals of the hydrogen atom (in the ≡C—H electron-accepting group), i.e. in the formation of π-complexes[33,34]:



The structure of the π-complex was subsequently refined by other investigators.

The existence of both π-complexes of acetylenic hydrocarbons and of a hydrogen bond between such hydrocarbons and the solvent has now been demonstrated. Hyong's studies[35] on hydrogen bonds in acetylenic compounds were published in 1963 in the form of a review. The review gives a detailed bibliography (153 references). A paragraph in Bellamy's familiar monograph (1968)[1] is devoted to the hydrogen bond in acetylenic hydrocarbons.

However, recently new data have appeared on the hydrogen bond in acetylenic compounds which are not quoted in the earlier publications. For example, the data of Iogansen and coworkers[36-38] concerning the nature and spectroscopic manifestations of the hydrogen bond,

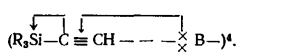
data for the hydrogen bond in acetylenic compounds containing Group IV atoms, and others. In his treatment of studies on the hydrogen bond, Bellamy [1] devoted insufficient attention to investigations published in Russian. We should like to fill this gap.

1. Effect of Molecular Structure on the Vibration Frequency Shift in the Formation of the Hydrogen Bond

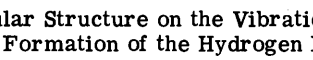
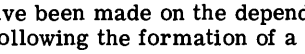
The first infrared spectroscopic evidence for the existence of a specific interaction in acetylenic hydrocarbons was obtained by Shuvalova [41], Murash et al. [42], Gastilovich et al. [43], Hyong and Lastondi [44], and Iogansen and Kurkchi [36,37]. They observed, using infrared spectra, a shift in the equilibrium between free and associated molecules of acetylenic hydrocarbons as a function of temperature and concentration of the solution.

Many studies have been made on the dependence of the band shift $\Delta\nu_{\equiv CH}$ following the formation of a hydrogen bond by acetylenic compounds on the structure of the R—C≡CH and solvent molecules [1,4,35,45-49].

Table 4 gives a compilation of certain data concerning the changes in the vibration frequency of the ≡CH group in acetylenes R—C≡CH of different structures dissolved in electron-donating solvents. Experimental studies have shown that an increase of conjugation in R—C≡CH molecules increases the $\Delta\nu_{\equiv CH}$ shift. Shigorin [52] explains this phenomenon by the fact that charge transfer on hydrogen bond formation is not localised at the A—H---⨯B- group but induces an additional change of electron density in all the rest of the electron-acceptor molecule. Electrons in the donor molecule ⨯B—R occupy the vacant p orbitals of the hydrogen atom and are therefore capable of participating in conjugation. Thus the increase of the $\Delta\nu_{\equiv CH}$ shift in both silyl- and arylacetylenes compared with the alkyl and stannyl derivatives can be accounted for by this type of conjugation:



Iogansen [39,53] has developed logically the concept of the additive influence of the acidity and basicity of the A—H and ⨯B—R components in the formation of a hydrogen bond. A somewhat different approach to the treatment of electron-donating properties of the solvent has been proposed by Plotnikov and Shigorin [54]. They suggested that the involvement in conjugation of the unshared electron pair of the donor in "its" molecule decreases the electron-donating capacity of the latter. For example, in nitrogen-containing electron-donating solvents, the $\Delta\nu_{\equiv CH}$ shift increases in the series R_2N-  ,  N, and $(C_2H_5)_3N$, while in oxygen-containing solvents it increases from acetone to dioxan [50].

The vibration frequency of the C≡C group changes little on formation of a hydrogen bond [35,55]. Molecules where the C≡C—H group is involved in conjugation constitute an exception. For example, in the spectrum of phenylacetylene and trimethylsilylacetylene dissolved in electron-donating solvents, two $\nu C\equiv C$ bands are observed ($\Delta\nu C\equiv C \simeq 7-12$ cm^{-1}), the intensity ratio of which changes with concentration [55]. These bands correspond to "free" and associated molecules in the R—C≡C—H—⨯B—R′ complex. The appearance in the spectrum of the solution of two $\nu C\equiv C$ bands makes it possible to calculate the degree of association in the hydrogen-bonded complexes from the intensity of the $\nu C\equiv C$ absorption band of the "free" molecule, as has been done on the basis of the $\nu_{\equiv CH}$ absorption band [48]. However, the splitting of the $\nu C\equiv C$ bands is not observed for all types of conjugation but only when the conjugation promotes further charge transfer from the  group to the R group of the acetylene. Otherwise, the splitting of $\nu C\equiv C$ is not observed. For example, spectroscopic data suggest a π-electronic interaction between the $R_2NCH=CH-$ and $-C\equiv C-H$ groups in the compound $R_2NCH=CH-C\equiv CH$ (Gastilovich et al. [15]); chemical data demonstrate a high reactivity of the C≡C group in this compound [56]. However, the $\Delta\nu_{\equiv CH}$ shift in the spectra of solutions of this compound in electron-donating solvents is the same as in alkylacetylenes (or smaller) and the $\nu C\equiv C$ band is not split (a different type of conjugation is postulated here: ) [57].

2. π-Complexes

The hypothesis of the formation of π-complexes between acetylenic compounds has been confirmed experimentally by Murash et al. [42], Shuvalova [58], and others [1,35]. When π-complexes are formed, the $\nu_{\equiv CH}$ vibration frequency changes very little, by approximately 20 cm^{-1} (Table 4), while the change in the vibration frequency of the C≡C group [35,55] is even smaller (1–2 cm^{-1}). However, as for the hydrogen bond of the type R—C≡C—H---⨯B—R′, two $\nu_{\equiv CH}$ bands are observed in the spectrum of the solution, corresponding to free and associated molecules. It has been shown [59] that the π-complex is T-shaped and that not one but two $\nu_{\equiv CH}$ frequencies are due to the bound molecules.

The electron-donating properties of the C≡C groups in various acetylenic compounds were studied by West and Kreihancel [60] and Hyong [35] using changes in the vibration frequency of the O—H groups of phenol and p-chlorophenol respectively. Similarly the electron-donating properties of the C≡C groups in certain silyl- and stannyl-acetylenes [8] have been determined from the changes in the vibration frequency of the O—H group of ethanol in the complex

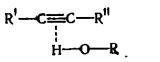


Table 5 presents some data for the electron-donating properties of the C≡C groups of various ethynyl compounds. Hyong [35] determined the energy of formation of the π-complex with p-dichlorophenol from the temperature variation of the degree of association. It varies in the range 2–3 kcal mole^{-1} for different acetylenes. Hyong showed that the π-electron-donating properties increase in the series alkenes < aromatic hydrocarbons < alkynes. According to the data of West and Kreihancel [60], the electron-donating properties of the C≡C group are more marked in disubstituted acetylenes compared with monosubstituted derivatives, and in the latter they decrease when the triple bond is conjugated with a ring. In disubstituted tin and silicon-containing acetylene derivatives (RXC≡CXR′), the electron-donating properties weaken in the series with X = Sn, C, and Si (Table 5).

Table 4. Vibration frequencies of the ≡C—H group ($\nu_{\equiv CH}$, cm^{-1}) in the infrared spectra of solutions of compounds of the type R—C≡CH.

Solvent or state of aggregation	Refs.35-38, 43, and 50				Refs.48 and 50	Ref.50	Ref.50	Ref.45	Ref.43	Ref.50	Ref.4	Ref.48	Refs.4 and 48
	R=H	CH_3	C_2H_5	C_3H_{10}	$(CH_3)_3C$			H—C≡C—	C_4H_9O—CH=CH—	$(C_2H_5)_2N$ CH=CH—	$(CH_3)_3Si$	$(CH_3)_2$ Si=	$(C_2H_5)_3Sn$
	$\nu_{\equiv CH}$ and $\Delta\nu_{\equiv CH} = \nu_{\equiv CH}$ (in CCl_4) $-\nu_{\equiv CH}$ (in electron-donating solvent)												
CCl_4	3263	3314	3313	3313	3312	3312	3312	3311	3310	3315	3285	3293	3276
Acetone $(CH_3)_2C=O$	3218 45	3273 41	3270 43	3273 40	3273 39	3260 52	3250 62	3239 72	3263 47	3280 35	3235 50	—	3232 44
Pyridine 	—	3228 85	3225 88	3254 79	3233 79	3215 97	—	—	3195 115	3250 65	3185 100	3186 107	3202 74
Tiethylamine $(C_2H_5)_3N$	—	—	—	3206 107	3204 107	3175 137	—	—	—	3190 125	—	3156 137	3182 94
Liquid	Tв.[51] 3276 3258	3295 18	3295 18	3292 21	3290 22	3290 32	3293 19	—	3290 20	3300 15	3279 6	3282 9	3258 18

*The compound $(CH_3)_2Si(C\equiv CH)_2$.

Table 5. The electron-donating properties of the C≡C group. Variation of the vibration frequencies of the O—H groups ($\Delta\nu$, cm^{-1}) in compounds of the type R—OH forming a π-complex with acetylene derivatives in CCl_4 solution.

ROH	Compound	$\Delta\nu_{OH}$	ROH	Compound	$\Delta\nu_{OH}$
C_6H_5OH (Ref.60)	$C_4H_9C\equiv CH$	90	C_2H_5OH (Ref.8)	$(CH_3)_3C-C\equiv C-CH_3$	71
	$C_3H_7C\equiv CC_3H_7$	137		$(CH_3)_3SiC\equiv CH$	39
		41.80*		$(CH_3)_3Si-C\equiv C-Si(CH_3)_3$	64
		44.108*		$(C_2H_5)_3Sn-C\equiv C-Sn(C_2H_5)_3$	107

*$\Delta\nu_{OH} \simeq 40\ cm^{-1}$ corresponds to a π-complex with the benzene ring.

3. The Lateral Band

In all ethynyl compounds, a weak ν_X band, which does not disappear on dilution of the solution, is observed on the long-wavelength side of the absorption band of the ≡CH group. Its nature has been investigated in numerous studies[1,35]. The appearance of the ν_X band is explained in Bellamy's monograph by Fermi resonance. Kreihancel and West[61] and Hyong[35] interpret this band as due to a hot transition in alkylacetylenes: $\nu_X = \nu_{\equiv CH} + \delta_{\equiv CH} - \delta_{\equiv CH}$. The ν_X band has a low intensity (the optical density ratio $D_X/D_{\equiv CH} \simeq 0.10$), is displaced relative to $\nu_{\equiv CH}$ towards longer wavelengths by about 20 cm^{-1}, and persists in the spectra of deuteriated compounds. At different temperatures, the intensity ratio of the $\nu_{\equiv CH}$ and ν_X bands varies in accordance with the calculated population of the "hot" $\delta_{\equiv CH}$ vibration level. In the spectrum of phenylacetylene, this additional band on the long-wavelength side (ν_C) is very intense ($D_C/D_{\equiv CH} \simeq 0.70$). Hyong[35] interprets its appearance by the Fermi resonance of the $\nu_{\equiv CH}$ and ν_C vibrations in a manner analogous to the interpretation of the ν_X band by Evans and Nyquist in the spectra of alkyl-substituted derivatives[62]. The latter postulate that $\nu_X = \nu_{C\equiv C} + 2\delta_{\equiv CH}$ or $\nu_{C\equiv C} + \delta_{\equiv CD}$ in deuteriated derivatives of acetylene. In a recent study, Bagdanskii et al.[51] studied the infrared spectra of acetylene in matrices at low temperatures. The band with a maximum at 3312 cm^{-1} (argon matrix) was interpreted as due to the $\nu_{C\equiv C} + \delta_{\equiv CH}$(i.r) + $\delta_{\equiv CH}$(Raman) = 1973.5 + 737 + 612 cm^{-1} transition intensified by Fermi resonance with the $\nu_{\equiv CH}$(i.r) = 3289 cm^{-1} vibration. The longer-wavelength band with a maximum at 3276 cm^{-1} was assigned to the $\nu_{\equiv CH}$ vibration (i.r) of the $^{12}C^{13}CH_2$ molecule. However, the authors noted that in this region there is a possibility of absorption by acetylene polymers.

The weak lateral bands ν_X are also observed in the spectra of dilute solutions of acetylenic compounds containing silicon and tin. In the latter [$(C_2H_5)_3Sn-C\equiv CH$], there are weak bands on the long-wavelength and short-wavelength sides of the main band (Table 6).

4. Spectroscopic Three-Atom Model of the Hydrogen Bond

The intensities of the absorption bands due to the ≡CH and C≡C groups in hydrogen-bonded complexes have been determined in a few studies. Brand et al.[63] observed a change (in different directions) of the stretching ($\nu_{\equiv CH}$) and deformation ($\delta_{\equiv CH}$) vibrations in hydrogen-bonded complexes as well as of the intensities of the corresponding absorption bands. Systematic studies of the $\nu_{\equiv CH}$ and $\delta_{\equiv CH}$ vibration frequencies and of the intensities of the absorption bands in different electron-donating solvents have been made by Iogansen and Kurkchi for acetylene and its alkyl-substituted derivatives[36-38,64]. Table 7 presents data for the changes in the intensity of the C≡C—H absorption band intensities on formation of a hydrogen-bonded complex with a solvent by certain acetylenic compounds of different structures.

On the basis of data showing that the $\nu_{\equiv CH}$ and $\delta_{\equiv CH}$ bands vary regularly in opposition and that $\Delta\nu_{\equiv CH}$ and $\Delta\delta_{\equiv CH}$ shift in opposite directions on formation of the hydrogen bonds, it was concluded [36-38,64] that the hydrogen bond is covalent. Using these concepts, Iogansen proposed a three-atom model for the formation of the hydrogen bond [39]. The model is based on the hypothesis that the charge transferred from the atom of the electron donor $\overset{\times}{}$B to the R—AH molecule is not delocalised over the latter. As a result, the change in the intensity of the absorption bands in the infrared spectra of the hydrogen-bonded complexes is caused by a change of the dipole moment of the H---B hydrogen bond itself during the vibration of the hydrogen atom and not due to a change in the dipole moment of the A–H bond.

Table 6. Positions of the absorption bands of the ≡CH group ($\nu_{\equiv CH}$) and the lateral ν_X bands (cm^{-1}) and their relative intensities (at the absorption maximum) $D_X/D_{\equiv CH}$ in the infrared spectra of compounds of the type R—C≡C–H (D) in carbon tetrachloride solutions [35].

	R										
	C_4H_9—	C_6H_{13}—	C_7H_{15}	C_7H_{15}— (D)*		 (D)*	$(CH_3)_3C$—	$(CH_3)_3Si$—	$(C_6H_5)_3Sn$-**	$(C_6H_5)_3Sn$ (D)*	
$\nu_{\equiv CH}$	3315	3314	3313	2598	3313	2594	3312	3292	3290	2567	3288
ν_X	3296	3294	3294	2584	3302	2584	3293	3274	3270, 3310	2553	3270
$\nu_X - \nu_{\equiv CH}$	—19	—20	—19	—14	—11	—10	—19	—18	—20 +20	—14	—18
$\frac{D_X}{D_{\equiv CH}}$	0.12	0.10	0.11	0.18	0.81	—	0.15	0.10	0.09 0.09	0.19	0.12

*The compound R—C≡C—D.
**Solution in hexane.

In the $\nu_{\equiv CH}$ stretching vibration in the "free" R–C≡CH molecule, only the hydrogen atom is displaced from the equilibrium position (the displacements of the C atoms may be neglected). Then, in accordance with the valence-optical scheme [25], the absolute intensity of the $\nu_{\equiv CH}$ absorption band ($B^{(0)}_{\nu CH}$) is related to the amplitude of the vibration of the ≡CH—H bond (q) and the derivative of the dipole moment of the molecule M with respect to the normal coordinate q by the expression const. $(B^{(0)}_{\nu CH})^{1/2} \simeq -(\partial M/\partial q)q$. When the C≡C—H---$\overset{\times}{}$B—R complex is formed, one can assume that the ≡C and B atoms are stationary and that hydrogen vibrates between them. Then the vibration amplitude q_{H---B} is equal to q but with the sign reversed, i.e. $q_{H---B} = -q$. The dipole moment changes in the –H--$\overset{\times}{}$B– bond vibration:

$$(\partial\mu_{H---B}/\partial q_{H---B})q_{H---B}.$$

The intensity of the absorption band of the hydrogen-bonded complex ($B^{(C)}_{\nu CH}$) is in this case determined by the two components: const. $(B^{(C)}_{\nu CH})^{1/2} = (\partial M/\partial q)q + e(\partial\mu_{H---B}/\partial q_{H---B})(q_{H---B})$. It is readily seen that the difference $(B^{(C)}_{\nu CH})^{1/2} - (B^{(0)}_{\nu CH})^{1/2} = \Delta(B^{1/2}_{\nu CH})$ for such a model depends only on the change in the dipole moment of the H---B bond during the vibration: $\Delta(B^{1/2}_{\nu CH}) \simeq (\partial\mu_{H---B}/\partial q_{H---B})q_{H---B}$.

Similarly, for deformation vibrations, $(B^{(C)}_{\delta})^{1/2} - (B^{(0)}_{\delta})^{1/2} = \Delta(B^{1/2}_{\delta}) \simeq (\mu_{H---B}/\rho_{H---B})\Delta e_{\equiv CH}$ (according to the valence-optical theory [24,25]), where ρ_{H---B} is the length of the H---B bond and Δe is the change of direction of the unit vector of the ≡C—H bond in the $\delta_{\equiv CH}$ vibration. Data for the changes in the frequency and intensity of the absorption bands of the C≡CH group led to the conclusion [64] that the derivatives $\partial M/\partial q$ and $\partial\mu_{H---B}/\partial q_{H---B}$ are of the opposite sign, while the dipole moments μ_q and μ_{H---B} have the same direction.

Table 7. The frequencies (cm^{-1}) and intensities B (in units of 10^4 cm^{-2} litre $mole^{-1}$) of the absorption bands of the stretching and deformation vibrations of the C≡C—H group in the spectra of compounds of the type R—C≡C—H in solutions in an inert solvent (O) and an electron-donating solvent (C).

	R											
	C_4H_9— [38]		$(CH_3)_3C$— [46]		[38,47]		$H_2C{=}CH$— [38]		$(CH_3)_3Si$— [47]		$(C_6H_5)_3Sn$— [48]	
	O	C	O	C	O	C	O	C	O	C	O	C
$\nu_{\equiv CH}$	3313 * 3319	3233 * 3308 3234	3312 3293	3228	3312 3321 [47]	3215 3211	3316	3220	3292 3274	3185	3310 3290 3270	3202
$B_{\nu CH}$	0.62 * 0.61	1.46 * 1.46	0.75	1.3	1.09 [47] 0.96 [38]	3.3 3.67	0.64	2.39	0.46	2.9	0.38	1.46
$\sigma_{\equiv CH}$	633	693	629	—	612, [38] 649	—	629	—	673	—	665	—
B_{δ}	0.93	1.1	1.2	—	1.01 [38]	—	0.94	—	1.0	—	1.2	—
$\nu_{C\equiv C}$	2121	2119 [35]	2105 2137	2103 2135	2112 [38]	2103	—	—	2033	2027	2008	1998
$B_{\nu C\equiv C}$	0.069	0.048 [35]	0.075	0.026	0.044	0.042	—	—	0.29	0.40	0.11	0.16

Note. Kurkchi and Iogansen [38] used iso-octane and carbon tetrachloride (distinguished by an asterisk) as the inert solvent (IS) and methylpyrrolidone or pyridine (asterisk) as the electron-donating solvent (EDS) and the corresponding values of B are quoted without taking into account the degree of association: Hyong [35] used carbon tetrachloride as IS and pyridine as EDS and the B are quoted without taking into account the degree of association; Gastilovich and coworkers [47,48] used carbon tetrachloride as IS and pyridine as EDS and the B are quoted with allowance for the degree of association.

The three-atom model of the covalent hydrogen bond discussed above have been confirmed by certain experiments. Thus the experimental intensities of the absorption bands corresponding to the vibrations of other bonds and the values calculated using the parameter $\partial\mu_{H---B}/\partial q_{H---B}$ agreed satisfactorily. For example, $(B^{(C)}_{\nu C\equiv C}) = 0.02 \times 10^4$ cm^{-1} litre $mole^{-1}$ was calculated for the $\nu_{C\equiv C}$ vibration frequencies of acetylene in the complex with acetone, the measured value being $B^{(C)}_{\nu C\equiv C} = 0.08 \times 10^4$ cm^{-1} litre $mole^{-1}$. [65]

5. Limitations of the Three-Atom Model

However, certain experimental data show that the three-atom model is apparently valid only to a first approximation and holds for A–H molecules in which the degree of conjugation of the donor electrons with the remainder of the A molecule is low. In molecules where there is such conjugation (R–C≡C–H---B), one cannot neglect the change in electron density in the remainder of the molecule on formation of the hydrogen bond. For example, an observation such as that of the appearance of two $\nu C{\equiv}C$ absorption bands in the spectra of the hydrogen-bonded complexes of certain acetylenic compounds contradicts the three-atom model discussed above. A numerical estimate shows that the vibration frequency of the C≡C group in the hydrogen-bonded complex may change only as a result of a change in the force constant K_Q. On the other hand, a change in the force constant of the ≡CH bond on formation of the hydrogen-bonded complex ($\Delta K_q \simeq -1.0 \times 10^6$ cm^{-2}) cannot change the $\nu C{\equiv}C$ vibration frequency[47] to such an extent (by about 10 cm^{-1}), despite the fact that the vibration mode of the latter is characteristic of the entire X–C≡C–H group.

The inadequacy of the three-atom model has been pointed out by Gastilovich et al.[47], who measured the intensities of the absorption bands due to the ≡CH and C≡C groups in certain acetylene derivatives in various solvents. Taking into account the $\nu{\equiv}CH$ and $\nu C{\equiv}C$ vibration modes and using the parameter $\partial\mu H\text{---}B/\partial q H\text{---}B$, the intensities of the C≡C absorption bands were calculated[47,48] from the relations

$$\left(\frac{\partial M}{\partial Q_{\equiv CH}}\right)_c = \left(\frac{\partial M}{\partial Q_{\equiv CH}}\right)_0 - 0.90\frac{\partial \mu_{H\text{---}B}}{\partial q_{H\text{---}B}} e_{\equiv CH},$$
$$\left(\frac{\partial M}{\partial Q_{C\equiv C}}\right)_c = \left(\frac{\partial M}{\partial Q_{C\equiv C}}\right)_0 - 0.24\frac{\partial \mu_{H\text{---}B}}{\partial q_{H\text{---}B}} e_{\equiv CH}, \quad (4)$$

where $Q{\equiv}CH$ and $QC{\equiv}C$ are the normal coordinates of the $\nu{\equiv}CH$ and $\nu C{\equiv}C$ vibrations respectively; $(\partial M/\partial q{\equiv}CH)[D/Å] = 1.6 \times 10^{-2} (E\nu CH)^{1/2}$, and a similar expression holds for $B\nu C{\equiv}C$, E being measured in cm^{-2} litre mole^{-1}. A discrepancy has been found between the calculated and experimental intensities of the $\nu C{\equiv}C$ bands in the spectra of the hydrogen-bonded complexes of phenylacetylene and trimethylsilylacetylene. The discrepancy has been attributed to a change in the electro-optical parameter of the C≡C bond ($\partial\mu X\text{–}C{\equiv}C\text{–}H/\partial Q$) on formation of the hydrogen bond, which is inconsistent with the three-atom model. However, for alkylacetylenes and certain silyl- and stannyl-acetylenes, the calculated and experimental intensities agree within the limits of experimental error. This finding can be explained by the weak conjugation in molecules with this structure[48].

The intensity of the C≡C absorption band decreases on formation of the hydrogen bond in aryl- and alkyl-acetylenes[35,47,55] and increases in silyl- and stannyl-acetylenes[47,48] (Table 7). It has been shown[5,14] that the dipole moments for the transition of the $\nu{\equiv}CH$ and the $\nu C{\equiv}C$ vibrations have opposite directions in alkylacetylenes and the same directions in silyl and stannyl derivatives ($R_3X\text{–}C{\equiv}CH$). On this basis, the opposite sign for the change in the intensity of the $\nu C{\equiv}C$ band in the spectra of these compounds on hydrogen bond formation has been explained from the standpoint of Iogansen's three-atom model (zeroth approximation) and on the hypothesis of conjugation in the C≡C–H models involving the electrons of the donor B (next approximation)[49]. Thus the parameter $\partial\mu X\text{–}C{\equiv}C\text{–}H/\partial Q$ for phenylacetylene and trimethylsilylacetylene dissolved in an inert solvent has the same sign. The change of this parameter for substances dissolved in an electron-donating solvent is also of the same sign. For example, $\Delta(\partial\mu X\text{–}C{\equiv}C\text{–}H/\partial Q) \simeq -0.9$ for pyridine.

Table 8. The dipole moments μ_q of the ≡C–H bond and their derivatives $\partial\mu_q/\partial q$ based on the infrared spectroscopic data for solutions of compounds of the type R–C≡CH in carbon tetrachloride and the changes in vibration frequencies (wave-numbers) $\Delta\nu{\equiv}CH = \nu{\equiv}CH$ (solution in CCl_4) – $\nu{\equiv}CH$ (solution in pyridine).

R–C≡C–H	μ_q, D	$\partial\mu_q/\partial qD/Å$,	$\Delta\nu_{\equiv CH}$, cm^{-1}
HC≡CH[1]	1.10	0.90	—
$(CH_3)_3SiC{\equiv}CH$	1.12±0.06	0.97	—100
$(CH_3)_3C\text{–}C{\equiv}CH$	1.[illegible]±0.05	1.22	—80
$(C_2H_5)_2N(CH_2)_2OCH{=}CH\text{–}C{\equiv}CH$	1.28±0.07	1.26	—85
	1.27±0.07	1.56	—97
$(C_2H_5)_2NCH{=}CH\text{–}C{\equiv}CH$	1.42±0.1	1.50	—65
$(C_2H_5)_3Sn\text{–}C{\equiv}CH$	1.3±0.2	0.85	—74

The stretching and deformation vibrations of the ≡C–H group in acetylene derivatives are characteristic as regards mode. Therefore the intensity of the absorption bands associated with these vibrations in the spectra of solutions in an inert solvent is proportional to the derivative of the dipole moment of the ≡C–H group with respect to the coordinate q, i.e. $\partial\mu_q/\partial q$, and to the dipole moment μ_q of the ≡CH bond respectively. Thus information about the distribution of electron density in the ≡C–H group may be obtained from the infrared spectrum. Table 8 lists the values of $\partial\mu_q/\partial q$ and μ_q for various compounds R–C≡CH,[8] obtained from measurements of the intensity in the spectrum of the solution in an inert solvent. These parameters have been compared with the shift of the $\nu{\equiv}CH$ band in the spectrum of the solution in pyridine. The data in Table 8 demonstrate the absence of a monotonic relation between the dipole moment, its derivative, and the capacity of the compounds R≡C–CH to form a hydrogen bond ($\Delta\nu{\equiv}CH$), which apparently indicates a limitation of the three-atom model.

6. Energy of the Hydrogen Bond

The spectroscopic determination of the energy of the hydrogen bond from the change in the degree of association with temperature yielded a fairly low value (1.5–2 kcal mole^{-1}).[35] The energy ΔH of the hydrogen bond between acetylene and its simplest alkyl derivatives on the one hand and an electron-donating solvent on the other has been determined[64] from the heat of solution. For example, $\Delta H = 1.4$ kcal mole^{-1} for the hydrogen-bonded complex with acetone and $\Delta H = 2.4$ kcal mole^{-1} for the complex with hexamethylphosphoramide.

Iogansen proposed a method for the determination of the hydrogen bond energy on the basis of the three-atom model of the hydrogen bond[40]:

$$\Delta H \text{ (kcal mole}^{-1}) = g\,[(B^{(c)}_{\nu CH})^{1/2} - (B^{(0)}_{\nu CH})^{1/2}] \qquad (5)$$

where the coefficient $g = 2.9$ hardly differs for different classes of A—H compounds. This method is very simple, since it does not require measurements at different temperatures. Only the intensity of the A—H(≡C—H) absorption band in the spectrum of the hydrogen-bonded complex and in the spectrum of the solution in an inert solvent is measured. According to the valence-optical scheme, the above relation presupposes a direct dependence of the hydrogen bond energy on the derivative of the dipole moment of the hydrogen bond itself with respect to the coordinate $q_{H\cdots B}$: $\Delta H \propto \partial\mu_{H\cdots B}/\partial q_{H\cdots B}$.

The energies of the hydrogen bond between acetylene and its alkyl derivatives on the one hand and the solvent on the other, determined from the absorption intensity and from the heat of solution, agree satisfactorily: $\Delta h = 1.1$ and 2.4 kcal mole^{-1} from the intensities in the infrared spectra in acetone and hexamethylphosphoramide solutions respectively (the data based on the heat of solution were given above). The hydrogen bond energies in alkyl-, stannyl-, and certain silyl-acetylenes ($R_3X—C\equiv CH$, X = C, Si, or Sn) in hydrogen-bonded complexes with pyridine have been determined from Eqn. (5)[48]. The hydrogen bond energy increases in the sequence X = C < X = Sn < X = Si: 1.2, 2.0, and 3.6 kcal mole^{-1}. However, in the light of the hypothesis concerning the hydrogen bond[52], discrepancies should be observed in certain systems between the hydrogen bond energies measured directly and those determined from the equation [Eqn. (5)] proposed by Iogansen. Such discrepancies may be expected for R—C≡C—H derivatives where the π electrons of the C≡C bond interact with the π electrons of the R—C≡C—H group, for example in $R_3Si—C\equiv CH$ and phenylacetylene.

IV. VIBRATIONAL (INFRARED) SPECTROSCOPIC STUDY OF INTRAMOLECULAR ELECTRONIC INTERACTION

As already mentioned in the introduction, conclusions concerning the mutual influence of various groups in the molecule cannot be reached solely on the basis of the experimental vibration frequencies and band and line intensities in the vibration spectra. The problem of applying vibration spectra in the study of polyatomic molecular structures is considered in the review of Gribov and Popov[66]. However, in the majority of spectroscopic studies where the problems of structures were examined this finding was ignored. For example, in the section dealing with spectroscopic studies in Luneva's review[2], the conclusions of the investigators quoted on the spectroscopic manifestation of π–d conjugation in molecules are discussed uncritically in this sense. Since the $\nu C\equiv C$ vibration does not show characteristic intensities and its frequency may vary within fairly wide limits [see Eqn. (2)] when the atom X in the X—C≡C—H group is varied, we shall not discuss here purely experimental studies devoted to the investigation of intramolecular interaction.

Certain conclusions about the mutual interaction of individual groups of atoms in the molecule can be reached by examining the force constants and electro-optical parameters of various molecules. However, we may note that these quantities may vary in different molecules both as a result of intramolecular interactions and as a result of a change of the hybridisation of the electrons forming the bonds under consideration. Moreover, since in the calculations on the vibrations the choice of the non-zero non-diagonal elements of the molecular force field is to some extent arbitrary, one cannot simply compare the force constant obtained by different investigators and arrive at conclusions concerning the change in the molecular force field on the basis of the differences between them. This is indicated by the data in Table 2. Finally the force constant itself and its changes in one direction or another for different molecules still cannot provide any information about the nature of the intramolecular interaction. A conclusion about the specific type of mutual interaction of groups in the molecule can be usually reached by considering data obtained in studies on the molecule by other methods. The problems of intramolecular interaction in acetylenic compounds have been discussed in a number of studies.[5,9–11,14,15,20–22,27,47,48,68]

1. Interaction with a Halogen and π–π Interaction

Lubuzh and Popov studied the effect of a halogen on the potential field of the ethynyl group[9]. Calculation on molecular vibrations showed that the replacement of hydrogen atoms in acetylene by the CH_3 group (methylacetylene) or Cl does not have an appreciable influence on the force (dynamic) constant of the C≡C—H group (Table 2).[9] In contrast to these groups, the remaining halogens (F, Br, and I) influence the ethynyl group. Thus in fluoroacetylene there is a sharp increase of the force constant of the C≡C bond ($K_Q = 27.2$) and of the dynamic interaction between the F—C≡ and C≡CH groups ($H^Q_{Q_1} = 1.09$). On the other hand, in bromo- and iodoacetylenes, $H^Q_{Q_1}$ decreases ($K_Q \simeq 25.5$) but the halogen does affect the ≡CH group: K_q decreases ($K_q = 10.4$). The results of this study are consistent with Duncan's data[12] for analogous compounds. Zerbi and Gussoni[13] showed that the halogen X separated from the C≡C—H group by a carbon atom ($H_2X—C—C\equiv CH$) does not alter the force constant of this group. However, the influence of the halogen distorts the cylindrical symmetry of the force field of the C≡C—H group and the spectra of these compounds show two bands corresponding to the δ≡CH deformation vibrations. Iodine has the greatest effect; the difference $K^{(1)}_\delta - K^{(2)}_\delta$ for this compound is high (about 0.09×10^6 cm^{-2}).

It has been shown[9,10,68] that the force constant of the C—C bond changes little (approximately by 10–15%) when the state of hybridisation of the electrons forming it alters: sp^3–sp^3, sp^3–sp^2, and sp^3–sp. The force constant is greatly influenced by the change in π-electron density: with increase of bond order K also increases. A considerable asymmetry of the force constants in the ≡C—O—C group was noted by Tenisheva et al.[20]: $K(\equiv C—O) = 13.6 \times 10^6$ cm^{-2} and $K(O—C) = 8.0 \times 10^6$ cm^{-2}. A similar phenomenon has been observed for silyl and stannyl derivatives of acetylene: $K(\equiv C—Si) = 5.7 \times 10^6$ cm^{-2} and $K(Si—C) = 5.1 \times 10^6$ cm^{-2} for the silyl derivative and $K(\equiv C—Sn) = 4.1 \times 10^6$ cm^{-2} and $K(Sn—C) = 3.60 \times 10^6$ cm^{-2} for the stannyl derivative[5,21]. However, in the latter the change in K can probably be accounted for mainly by a change in hybridisation.

Popov and coworkers carried out an interesting series of studies in which they established a definite correspondence between the type of force field and the nature of the intramolecular electronic interaction (conjugation). Popov and Lubuzh[22] determined the force field for diacetylene and dimethyldiacetylene. The force constant of the $\overset{Q}{C}\equiv\overset{q_0}{C}-\overset{Q'}{C}\equiv C$ groups (the designation of the normal coordinate is indicated above the bonds) for these molecules differ considerably from the corresponding values for the acetylene and methylacetylene molecules. Thus K_Q is appreciably reduced (24.1×10^6 cm^{-2}), K_{q_0} increases (12.8×10^6 cm^{-2}), and the dynamic constant for the interaction of triple bonds is also higher ($H^{Q}_{Q_1} = -1.64 \times 10^6$ cm^{-2}); $H^{Q}_{Q_0} = 0.54 \times 10^6$ cm^{-2}. The authors concluded that such a characteristic force field in the molecules investigated can be accounted for by electron delocalisation. They showed that the proposed set of force constants describes satisfactorily the vibration spectra of the polyacetylenes $R-(C\equiv C)_n-R$ with $n = 2-6$ in contrast to the set obtained by other workers. The form of the force field of polyacetylenes led the authors[22] to the conclusion that the interaction between the triple bonds in the $(C\equiv C)_n$ chain decays rapidly and that the phenomenon of bond order equalisation does not occur. Having examined the force fields of molecules with different types of intramolecular electronic interaction, Popov and Kogan[67] proposed a classification of molecular force fields, involving a subdivision into four types depending on the diagonal and non-diagonal elements, so that each type of force field corresponds to a definite type of distribution of electron density in the molecule. Popov and coworkers carried out calculations on the vibrations of vinylacetylene and its methyl-substituted derivatives[10] on the basis of the force field classification and quantum-mechanical calculations which showed a delocalisation of electron density in the molecules under consideration. The authors concluded that the satisfactory agreement among more than 120 calculated and experimental vibration frequencies confirms the data showing a delocalisation of electron density in such a molecule and the initial postulates that the type of force field and the electronic structure of the molecule correspond.

Epshtein and Popov[11] obtained a distinctive type of force field for the propynal molecule ($\overset{O}{\underset{H}{\diagdown\!\!\diagup}}C-C\equiv CH$): K_Q and $K(O=C)$ are reduced compared with acetylene and acetaldehyde, while K_{Q_1} is higher. The authors concluded that the type of force field of this molecule is consistent with quantum-mechanical calculations, which demonstrate a delocalisation of π electrons in this molecule.

Popov et al.[27] pointed out the similarity of the force constants and electro-optical parameters for the $C=C-C\equiv C$, $C=C-C=C$, and $C\equiv C-C\equiv C$ carbon chains, which they explained by the same cause in each molecule—a partial delocalisation of electron density. Thus the calculated electro-optical parameters of the carbon chain in the vinylacetylene molecule are non-zero and large, in contrast to the data for dimethylacetylene[29]. The authors concluded that these results indicate a polarisation of the $C=C-C\equiv C$ bonds in the molecule ($\underset{\sim}{C}=\underset{\sim}{C}-\underset{\sim}{C}\equiv\underset{\sim}{C}$). Calculation of the absorption band intensities in the spectrum of another substance (diacetylene) using the electro-optical parameters of vinylacetylene resulted in a satisfactory agreement between the calculated and experimental data.

2. Interaction Involving Groups Containing Si, Sn, N, O, and S Atoms

Gastilovich, Shigorin, and coworkers studied the mutual interaction of groups in acetylene derivatives containing silicon and tin as the X atom. The suggested electronic effects—the inductive effect and π–d conjugation–lead to the opposite changes in the distribution of electron density in the $Si-C\equiv CH$ and $Sn-C\equiv CH$ groups: $\begin{matrix}C\\ \downarrow\\ C\rightarrow X\rightarrow C\equiv C-H\\ C\end{matrix}$.

Calculations on the vibrations of the $C_3X-C\equiv CH$ groups in the $(CH_3)_3Si-C\equiv CH$ (Gastilovich et al.[5]) and $(C_2H_5)_3Sn-C\equiv CH$ (Gastilovich et al.[14]) groups showed that the dynamic constants K_Q and K_q for the compounds are smaller than for t-butylacetylene[5] $(CH_3)_3C-C\equiv CH$ (Table 2). The changes in the electro-optical parameters of these compounds can be seen from Table 3. The changes in the electro-optical parameters of the $X-C\equiv C-H$ groups and the almost constant value of the electro-optical parameter of the C_3-X group led the authors to the conclusion that the degrees of π-d conjugation in the silicon- and tin-containing compounds investigated are different[14]. The study of hydrogen bonding in these compounds showed that the electron-donating properties of the groups decrease in the sequence $Sn-C\equiv C-Sn > C-C\equiv C-C > Si-C\equiv C-Si$ and the electron-accepting properties of $R_3SiC\equiv CH$ are more pronounced than those of $R_3C-C\equiv CH$ and $R_3Sn-C\equiv CH$ (Tables 4 and 5). The authors concluded that the above findings indicate a shift of π-electron density in silylacetylenes from the $C\equiv C$ group to $\equiv C-Si$ (π-d conjugation) and an appreciably smaller degree of such interaction in stannylacetylenes.

Another approach has been proposed[47] for the study of the problem of conjugation, which is based on the hypothesis that the three-atom model of the hydrogen bond is inadequate for molecules where the intramolecular interaction takes the form of conjugation (see Section III, 5). Calculation of the absorption band intensities associated with the $\nu C\equiv C$ vibrations on formation of an intermolecular hydrogen bond with an electron-donating solvent showed that the calculation based on an additive scheme (three-atom model) yields satisfactory results for the stannylacetylene[48] $(C_2H_5)_3Sn-C\equiv CH$. However, the assumption of additivity for trimethylsilylacetylene[47] $(CH_3)_3SiC\equiv CH$ and also for phenylacetylene leads to a discrepancy between the calculated and experimental quantities owing to the neglect of conjugation. A similar experiment and calculation led the authors to the conclusion that in silyl derivatives with several ethynyl groups π-d conjugation diminishes. Shakhovskii et al.[69] believe that the shift of the electron cloud towards the silicon atom (which they explained by π-d conjugation) is indicated by the magnitude and the direction of the dipole moments of substances of the type $R_3SiC\equiv C-C\equiv CH$.

On the basis of NMR data and measurements of the molecular dipole moments, Petrov et al. concluded that there is intramolecular charge transfer from the nitrogen atom to the ethynyl group in the compound $R_2NCH=CH-C\equiv C-Si(CH_3)_3$.[70] Considerable changes in the intensities of the absorption bands associated with the $\nu C\equiv C$ and $\nu C=C$ vibrations are observed in the spectra of compounds of the type $RYCH=CH-C\equiv CH$ (Y = S, O, or N) as a function of the atom Y.[15,71,72] However, these changes arise mainly because the above vibrations do not have characteristic intensities[6,15]. It is suggested that there is an intramolecular interaction between

YCH=CH and −C≡C−H groups in such compounds on the basis of data showing that there is discrepancy between the experimental intensities and the values calculated assuming additivity [15]. Calculation of the intensities of the $\nu C{\equiv}C$ absorption bands in the spectra of the compounds $RYCH{=}CH{-}C{\equiv}C{-}Si(CH_3)_3$ from the $\nu C{\equiv}C$ band intensities in the spectra of the compounds $RYCH{=}CH{-}C{\equiv}CH$ and the electro-optical parameters of the $\equiv C{-}Si(CH_3)_3$ group showed a deviation from additivity only for compounds containing nitrogen. The authors concluded that other heteroatoms (S and O) have only a weak influence on the dynamic and electro-optical characteristics of the $=C{-}C{\equiv}C{-}H$ group.

Table 9. Vibration frequencies (wave-numbers) ν (cm^{-1}) and intensities B (in units of 10^4 cm^{-2} litre $mole^{-1}$) of the infrared absorption bands and I of the Raman lines [in relative units: $I_{313}(CCl_4) = 100$] in the spectra of compounds with several ethynyl groups.

Compound	Raman			Infrared			
	$\nu_{\equiv CH}$	$\nu_{C\equiv C}$	$I_{C\equiv C}$	$\nu_{\equiv CH}$	$B_{\equiv CH}$	$\nu_{C\equiv C}$	$B_{C\equiv C}$
$(CH_3)_3SiC{\equiv}CH$ (Ref.89)	3276	2040	141	3292 [90]	0.46	2035	0.25
$(CH_3)_2Si(C{\equiv}CH)_2$	3268	2046	292	3294	1.16	2043	1.0
$CH_3{-}Si(C{\equiv}CH)_3$	3270	2044	426	3288 *	1.80	2046	1.32
$Si(C{\equiv}CH)_4$	3268	2050	590	3296	2.56	2050	
				3290 *	—		1.52
$(C_2H_5)_3SnC{\equiv}CH$ [1]	3268	2008	161	3287 [14]	0.45	2005	0.10
$(C_2H_5)_2Sn(C{\equiv}CH)_2$				3293 [21]	0.89	2017	0.31
$C_2H_5Sn(C{\equiv}CH)_3$				3296	1.35	2019	0.60
$(C_6H_5)_3SnC{\equiv}C{-}C_6H_5$ (Ref.92)	—	2137	2000				
$(C_6H_5)_2Sn(C{\equiv}C{-}C_6H_5)_2$	—	2148	3260				
$Sn(C{\equiv}C{-}C_6H_5)_4$	—	2154	6560				

*Solution in CS_2.

A considerable mutual influence of the C≡C and ≡C−Sn groups (in contrast to CAlk−Sn) was also detected by calculating the electro-optical parameters of tin-containing compounds with several ethynyl groups [21]. However, we may note that a similar interaction has been observed also for H−C bonds in the methyl group [25].

Among purely experimental studies, mention should be made of those of Buchert, Zeil, and Haals [73-75], Sacher, and coworkers [76,77], and Miller and Lemmon [78], who quote the vibration frequencies of the molecules investigated and give their interpretation [for the compound $R_3SiC{\equiv}C{-}X$ with X = H, $Si(CH_3)_3$, or Hal, $H_3C{-}X(C{\equiv}C{-}H)_3$ and $X(C{\equiv}CH)_4$ with X = Si, Ge, or Sn, and $Y(C{\equiv}CH)_3$ with Y = P, As, or Sb]. The characteristic frequencies of compounds containing Group IV and V elements can be found in the reviews by Chumaevskii and coworkers [79,80]. In the majority of other experimental studies, certain vibration frequencies and absorption bands or line intensities were considered and the specific changes in these quantities for various molecules were explained by changes in the distribution of electron density in the XC≡CX′ group (see, for example, Refs. 71-72 and 81-88). However, examination of the vibrations of the ethynyl group (Section I of the present review) shows that the authors' conclusion concerning the electronegativities of various atomic groups, conjugation, vacant orbitals, and the activity of the lone electron pairs of various atoms are in the majority of cases groundless. However, these studies contain rich and remarkable experimental data. For example, there is an interesting variation of the absorption and line intensities in the infrared and Raman spectra corresponding to the $\nu C{\equiv}C$ vibration (Table 9) with the number of ethynyl groups. Thus in the Raman spectra the intensity increases in proportion to the number of these groups, which is not the case in the infrared spectra.

Table 10. Effect of molecular structure on the $\nu C{\equiv}C$ vibration frequency and the intensity B (in units of 10^4 cm^{-2} litre $mole^{-1}$) of the infrared absorption bands or I of the Raman lines (in relative units*).

Chemical formula	$\nu_{C\equiv C}$, cm^{-1}	$B_{C\equiv C}$ or $I_{C\equiv C}$	Method	References
$n\text{-}C_4H_9{-}C{\equiv}CH$	2120	0.067	i.r.	83
$(C_2H_5)_3Ge{-}C{\equiv}CH$	2027	0.10		
$(C_2H_5)_3Ge{-}CH_2{-}C{\equiv}CH$	2112	0.20		
$(C_4H_9)_3Ge{-}C{\equiv}C{-}C_4H_9$	2166	0.47		
$(C_2H_5)_3Ge{-}C{\equiv}C{-}C{\equiv}C{-}C_2H_5$	2242	0.25		
	2103	0.25		
$(CH_3)_3Si{-}C{\equiv}C{-}C(CH_3)_2{-}C{\equiv}CH$	2206	90	R**	93
	2174	162		
$(C_2H_5)_3Si{-}C{\equiv}C{-}C_6H_5$		1360	R	91
$(C_2H_5)_3Sn{-}C{\equiv}C{-}C_6H_5$	2136	2324		
$(C_4H_9)_3Sn{-}C{\equiv}C{-}C_4H_9$	2151	170	R	91
$(C_4H_9)_3Sn{-}C{\equiv}C{-}C_4H_9$	2160	240		
$(C_6H_5)_3Sn{-}C{\equiv}C{-}CH{=}CH_2$	2138	755		
$(C_2H_5)_3Pb{-}C{\equiv}C{-}C_6H_5$	2132	—	i.r.	88
$C_4H_9SCH{=}CH{-}C{\equiv}CH$	2094	0.08	i.r.	71,90
$C_4H_9OCH{=}CH{-}C{\equiv}CH$	2100	0.18		
$(C_2H_5)_2NCH{=}CH{-}C{\equiv}CH$	2075	0.74		
$C_4H_9SCH{=}CH{-}C{\equiv}C{-}Si(CH_3)_3$	2140	0.74	i.r.	90
$C_4H_9OCH{=}CH{-}C{\equiv}C{-}Si(CH_3)_3$	2148	0.90		
	2134			
$(C_2H_5)_2NCH{=}CH{-}C{\equiv}C{-}Si(CH_3)_3$	2116	2.90		
$C_2H_5{-}CH(OH){-}C{\equiv}CH$	2112	60	R	94
	2110	0.022	i.r.	
$C_2H_5{-}C(=O){-}C{\equiv}CH$	2092	109	R	
	2093	0.52	i.r.	

*$I_{C\equiv C}$ in monoalkylacetylene was taken to be 100 units.

We shall complete the present review by a Table (Table 10) providing a clear illustration (together with Table 9) of the changes, which are sometimes enormous, in the frequency and particularly the intensity of the absorption band associated with the $\nu C{\equiv}C$ vibrations as a function of molecular structure. Unfortunately, these changes in the infrared spectra and apparently to an even greater extent in the Raman spectra do not characterise the changes in the distribution of electron density directly in the C≡C group.

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Karpov Physicochemical Institute,
Moscow

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The Determination of the Position of Double Bond in Unsaturated Steroids by Mass Spectrometry

N.S.Vul'fson and V.G.Zaikin

The possibilities and limitations of the mass-spectrometric method in the solution of problems concerning the location of the double bond in steroids have been demonstrated for a large number of such compounds containing the double bond in various positions in the polycyclic system and in the side chain. The mass spectra of Δ^1-, Δ^2-, Δ^4-, Δ^5-, Δ^7-, Δ^{13}-, Δ^{16}-, Δ^{22}-, Δ^{23}-, and Δ^{24}-steroids, in which the diagnostic fragments are due to the dissociation of at least one allylic bond, are the most characteristic. The double bonds in other positions in the steroid skeleton either do not initiate specific decomposition processes at all, or inhibit processes characteristic of the corresponding saturated analogues, or cause the appearance of fragments the driving force responsible for the formation of which is obscure. A separate section of the review deals with aromatic and diene steroids. The bibliography includes 86 references.

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I. INTRODUCTION

The determination of the position of the double bond in natural unsaturated steroids does not present much difficulty at present, since the steroids from hormones encountered in nature contain double bonds in a limited number of positions in the polycyclic system and in the side chain at $C_{(17)}$. However, this problem constantly faces investigators working in the field of the synthetic chemistry of steroids and also chemists dealing with the determination of the structure of various functional derivatives of natural steroids. In the latter case, when the positions of certain substituents, for example hydroxy-, alkoxy-, or acyloxy-groups, are determined, the problem is significantly facilitated when the location of the double bond formed as a result of the *trans*-elimination of these groups is known. Recently, mass spectrometry has been successfully employed to establish the position of the bond together with other physicochemical methods. The advantage of this method over others consists in its speed and extremely small amounts of substance required for analysis.

Attempts to employ mass spectrometry in order to establish the position of the double bond in aliphatic compounds were unsuccessful. As a rule, owing to the migration of the double bond under the influence of electron impact, peaks of the characteristic ions, the formation of which could be related to the position of the double bond, cannot be observed in the mass spectra of the corresponding compounds. The study of the mass spectra of the products of a transformation of unsaturated aliphatic compounds which fixes the position of the double bond, for example of the corresponding epoxides, is more promising. In cyclic compounds, including steroids, the double bond shows less tendency towards migration under the conditions of mass-spectrometric measurements and frequently initiates specific decompositions which can be used to determine its position. The formation of the majority of fragments arising under the influence of the double bond includes the dissociation of at least one allylic C—C bond. A special case of this process is the decomposition of the type of the retro-diene reaction (RDR) (or the "Diels—Alder retro-reaction"), which takes place with the dissociation of two allylic C—C bonds, and the charge may be located at the diene and or the so called dienophile fragment. Sometimes the process is accompanied by the migration of the hydrogen atom to the charged fragment or away from it. The relative intensities of the peaks corresponding to RDR depend on the stability of the ions formed. Decomposition of the RDR type was first described by Reed[1] and was subsequently analysed in detail by Biemann[2] and Djerassi and coworkers[3] for different types of unsaturated cyclic compounds. This type of fragmentation is interesting because, apart from the determination of the position of the double bond, the mass number of the corresponding ion frequently yields information about the nature of the substituent in the ring.

Among unsaturated steroids, compounds without functional substituents, such as keto-, hydroxy-, alkoxy-, and acyloxy-groups, or additional double bonds, are comparatively rarely encountered. Each of these functional groups can influence the decomposition of the molecular ion under electron impact and the problem of the determination of the double bond position in such cases is closely related to the determination of the nature and position of the substituent.

Numerous studies in which mass-spectrometric data for unsaturated steroids are given and discussed in different degrees of detail have now accumulated. However, there are comparatively few systematic studies in this field and many published investigations suffer from lack of a detailed analysis of the mass spectra quoted.

In the present review an attempt is made to give a systematic account of the accumulated mass-spectrometric determinations of the position of the double bond in unsaturated steroids. Studies in which the mass-spectrometric data quoted are insufficient to infer the influence of the

double bond on fragmentation under electron impact have been excluded from consideration.

One must stipulate beforehand that many of the decomposition mechanisms and ionic structures quoted in the review are of a formal kind and frequently have not been confirmed experimentally. However, such representation of mass-spectrometric processes is now generally adopted in the literature. On the other hand, the proposed mechanisms of decompositions under electron impact frequently find analogies in photochemistry, radiation chemistry, plasma chemistry, electrochemistry of organic compounds, and even solution chemistry. In representing the bond dissociations, we have employed three types of notation: homolytic dissociation is represented by a "hook", an arrow represented heterolytic dissociation, and a wavy line represents any of these dissociations when it is impossible to postulate a reasonably well founded mechanism.

II. STEROIDS WITH A DOUBLE BOND IN RING *A*

1. Δ^2-Steroids

One of the first studies dealing with the effect of the position of the double bond in steroids on the pathways in the decomposition of the molecular ion under electron impact was that by Audier et al.[4], who showed that decomposition via an RDR mechanism is characteristic of the type (A) Δ^2-steroid which they investigated (Table 1):

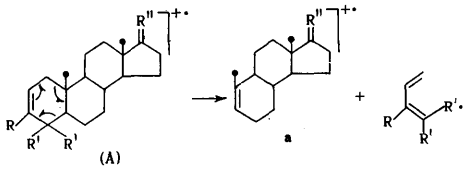
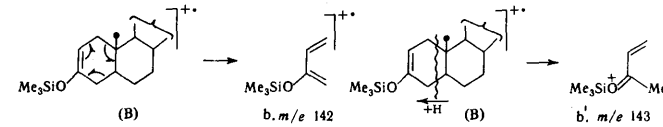


Table 1. The values of *m/e* (intensity expressed as a percentage of the maximum) for the ion a in the mass spectra of type (A) Δ^2-steroids[4]. *

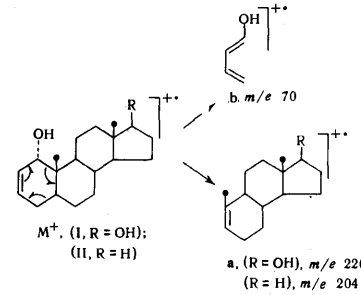
Compound	R	R′	R″	Diene eliminated	*m/e* for ion a
Androst-2-ene	H	H	H_2	Butadiene	$(M-54)^{+\cdot}$,204(91)
Cholest-2-ene	H	H	H, C_8H_{17}	Butadiene	$(M-54)^{+\cdot}$,316(65)
Androst-2-en-17-one	H	H	0	Butadiene	$(M-54)^{+\cdot}$,218(100)
3-Methylcholest-3-ene	Me	H	H, C_8H_{17}	2-Methylbutadiene	$(M-68)^{+\cdot}$,316(81)
Cholest-2-en-3-yl acetate	MeCOO	H	H, C_8H_{17}	2-Acetoxybutadiene	$(M-112)^{+\cdot}$,316(68)
3-Methoxycholest-2-ene	MeO	H	H, C_8H_{17}	2-Methoxybutadiene	$(M-84)^{+\cdot}$,316(38)
4,4-Dimethylcholest-3-ene	H	CH_3	H, C_8H_{17}	2-Methylpenta-2,4-diene	$(M-82)^{+\cdot}$,316(3)

* Audier et al.[4] do not quote the peak intensities of the type b diene ions.

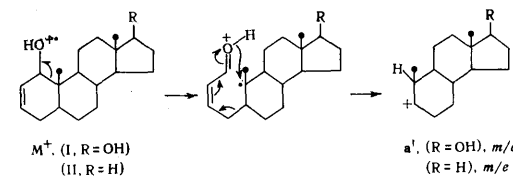
Peaks due to ions caused by the elimination of a diene as a rule predominate in the mass spectra of these compounds, while the ionic peaks of the dienes themselves are low. In the mass spectrum of 4,4-dimethyl-5α-cholest-2-ene the peaks of the dienophile fragment a amounts to only 3% of the maximum peak in the spectrum, while the intensity of the peak corresponding to the diene ion (*m/e* 82) is much higher. A similar situation is observed also in the spectrum of lanost-2-ene (4,4,14α-trimethyl-5α-cholest-2-ene).[5] Thus the introduction of a *gem*-dimethyl group in the 4-position partly stabilises the diene fragment. Table 1 shows that the RDR type of decomposition is characteristic also of enol acetates and enolic ethers. In type (B) 3-trimethylsilyloxy-Δ^2-steroids[6], this process leads to the preferential formation of the diene ion b with *m/e* 142 to which corresponds a rearranged ion with *m/e* 143 (b′).



In the mass spectra of androst-2-ene-1α,17β-diol (I) [7] and androst-2-en-1α-ol (II),[8,9] there are intense peaks due to ions **b** with *m/e* 70 (in both cases) and also of ions **a** with *m/e* 220 and 204 respectively due to the RDR type of decomposition:



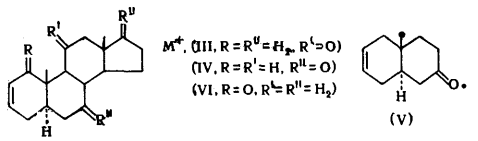
An important characteristic of spectra (I) and (II) is also the presence of peaks with *m/e* 221 and 205 (due to ions a′) respectively, which are much more intense than the peaks due to ions a and are formed with migration of a hydrogen atom to the charged fragment. The mechanism suggested[8,9] for the formation of ions a′,



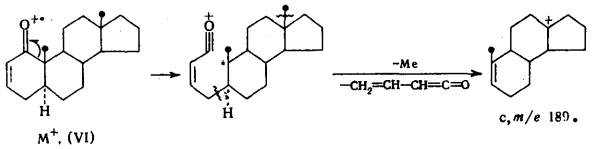
has not been confirmed experimentally.

It is interesting to follow the influence of the number and positions of carbonyl groups in Δ^2-steroids on their capacity to decompose via an RDR mechanism. The effect of carbonyl groups remote from the double bond may be considered for the following two examples. An intense peak due to an ion with *m/e* 218, $(M-54)^+$ formed by RDR in ring *A* accompanied by the ejection of a butadiene molecule, was observed by Djerassi and coworkers[10] in the mass spectrum of 5α-androst-2-en-11-one (III). In contrast there is no peak corresponding to RDR in the spectrum of 5α-androst-2-ene-7,17-dione (IV),[4] while in the spectrum of *trans*-10-methyl-2-octalone (V), which has a similar structure, the peak of the ion due to RDR is present[11]. We believe that this unusual behaviour of (IV) is associated with the possibility of the location of the charge at carbonyl groups remote from the double bond. This factor must be always borne in mind in the interpretation of the mass spectra, since ionisation of molecules "far" from the double bond can either greatly stabilise the molecular ion or can facilitate the occurrence of

competing reactions and thereby inhibit the processes initiated by the double bond:

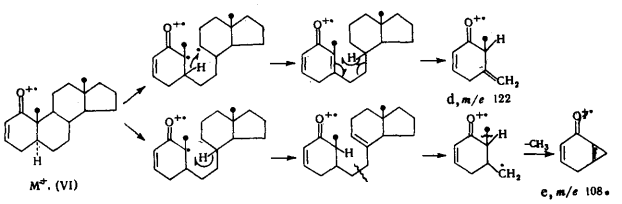


In the study of the decomposition of 5α-androst-2-en-1-one (VI) and its deutero-analogue (labelled at $C_{(2)}$, $C_{(4)}$, $C_{(5)}$, $C_{(6)}$, $C_{(7)}$, and $C_{(16)}$) under electron impact, Djerassi and coworkers[12] showed that the $C_{(2)}$ and $C_{(4)}$ atoms are eliminated from the neutral molecule on formation of an ion with *m/e* 189 (c) from the molecular ion. They proposed the following mechanism for the formation of the ion c:



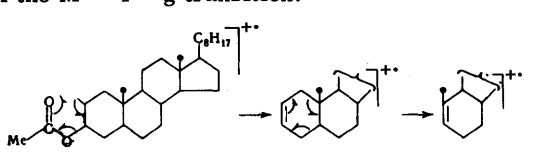
We suggest that the formation of the ion c can be due to an RDR type of decomposition with simultaneous elimination of one of the angular methyl groups.

Moreover, the spectrum of compound (VI) has peaks due to ions with *m/e* 122 (d) and 108 (e) the formation of which is interpreted as follows[12]:



The peak of the ion d with *m/e* 108 is accompanied by the peak of an ion with *m/e* 909 which is formed with migration of two hydrogen atoms, in contrast to the former.

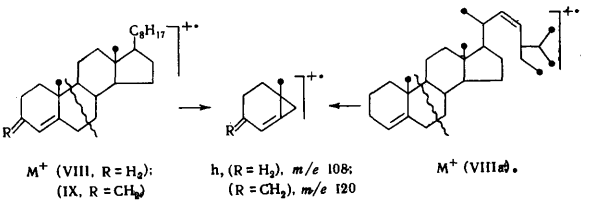
In connection with the discussion of the retro-diene reaction, which is characteristic of Δ^2-steroids, mention should be made of the capacity of such related 3-hydroxysteroids and particularly their acetates to undergo a type RDR decomposition after the elimination of the 3-OH or 3-$OCOCH_3$ groups in the form of water or acetic acid. In most cases the 1,2-elimination of these substituents is associated with a thermal process which leads to the formation of a Δ^2-steroid even before electron impact. Indeed in the spectrum of 5α-cholestan-3β-yl acetate (VII), recorded when the specimen was introduced at 250°C,[13] the peak of the M^+ ion is absent and the peak of the $(M - CH_3COOH)^+$ ion (e), which splits off butadiene as a result of RDR with formation of an *m/e* 316 ion (g), predominates in the mass spectrum. One cannot rule out the possibility that the ion f is formed to some extent also under electron impact. Thus the spectrum of compound (VII), recorded at 80°C,[14] shows all the peaks characteristic of the $M^+ \rightarrow f \rightarrow g$ transition:



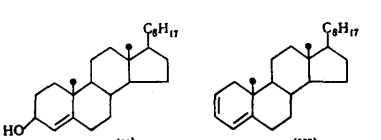
A similar sequence is observed also in the decomposition of the molecular ions from 5α-cholestan-3β-ol, coprostan-3β-ol, its acetate, and 4,4-dimethyl-5α-cholestan-3β-ol.[15] This feature of the fragmentation of saturated 3β-acetoxysteroids has been used[16] to establish the composition of a mixture of plant sterols subjected to preliminary hydrogenation and then acetylated. Butadiene is not split off from Δ^5-hydroxysteroids and their acetates[14], which also form readily $(M - 18)^+$ and $(M - 60)^+$ ions. This phenomenon is associated with the preferential formation of a conjugated 3,5-diene and not its 2,5-isomer.

2. Δ^4-Steroids

Among the simplest Δ^4-steroids without additional functional groups, cholest-4-ene (VIII) [17,18] and stigmasta-4,22-diene (VIIIa) [1] have been investigated. The peak of the ion with *m/e* 108 (h), which is the second most intense in the mass spectrum of compound (VIII), is due to the simple dissociation of the 6—7 and 9—10 allylic bonds[18]. An intense peak due to the ion h is observed also in the spectrum of compound (VIII).[1] A similar dissociation of 6—7 and 9—10 allylic bonds in 3-methylenecholest-4-ene (IX) [18] leads to an ion with *m/e* 120. The peak of this ion in the spectrum of compound (IX) is accompanied by equally intense peaks due to ions with *m/e* 106 and 94 the first of which may be formed as a result of the dissociation of 5—6 and 9—10 bonds:

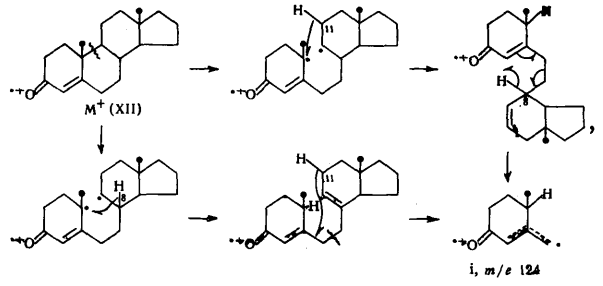


Proceeding now to steroids containing functional groups, we must consider in the first place the mass spectrum of allocholesterol (X).[17-19] The allocholesterol molecule shows an exceptional tendency towards thermal dehydration and therefore its spectrum, recorded using a hot glass inlet system at 200°C, does not contain the peak of the molecular ion and is absolutely identical with the spectrum of cholesta-2,4-diene (XI) (see section VII, 2). When the specimen is introduced directly into the ion source, which makes it possible to reduce the experimental temperature to 90—100°C, a large peak due to the molecular ion and the fragments resulting from its subsequent decomposition appears in the spectrum of compound (X), but a very significant feature of this spectrum is still the decomposition characteristic of compound (XI).

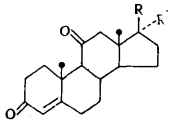


The most extensive and interesting data have been obtained in mass-spectrometric studies on Δ^4-3-ketosteroids. Shapiro and Djerassi[20] were the first to demonstrate for androst-4-en-3-one (XII) an important characteristic of the decomposition of such systems. It was found that the main peak in the mass spectrum of compound (XII) corresponds to the ion i with *m/e* 124. It was shown with the aid of the mass spectra of 2,2,4,6,6-D_5-, 8-D_1, 11,11-D_2-, and 19-D_1-analogues of compound (XII), its 7β-D_1-17β-OH-analogue, and also the

spectrum of cholest-4-en-3-one (XIII) that the ion i contains the *A* ring, the 19-CH_3 group, and a $C_{(6)}$ atom, being formed as a result of the dissociation of 6—7 and 9—10 allylic bonds with transfer of two hydrogen atoms from $C_{(8)}$ and $C_{(11)}$ to the charged fragment, as shown in the mechanism below[20,21]:



An additional piece of evidence of the validity of the mechanism proposed to account for the formation of the ion i is also the finding that in the mass spectra of androst-4-ene-3,11-dione (XIV),[20,22] cortisone (XV),[2,20,23-25], and androst-4-ene-3,11,17-trione (XVI) [24] a peak with *m/e* 122 due to the simple dissociation of the 6—7 and 9—10 bonds without the migration of hydrogen atoms appears instead of the ion i. This can be explained by the absence of hydrogen atoms at $C_{(11)}$ in compounds (XIV)—(XVI).

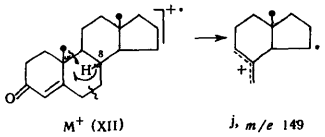


(XIV, R = R' = H);
(XV, R = $COCH_2OH$, R = OH);
(XVI, R + R' = O)

The presence of the peak due to the ion i and its analogues, the mass number of which depends on the substituents in ring *A* and at $C_{(6)}$ and $C_{(19)}$ is common to the mass spectra of all steroid Δ^4-3-ketones and can be used for their identification (Table 2).

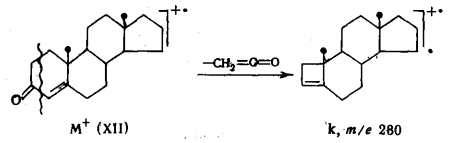
The ion i and its analogues are formed directly from the molecular ion and therefore their peak intensities are related. In the spectra of compounds containing, for example, functional groups which are readily eliminated by electron impact, the molecular ion peaks are small or altogether absent. At the same time there is a significant decrease of the peak due to the ions i. However, the peaks of these ions and their analogues with even mass numbers, can be as a rule reliably detected in the spectrum, since groups of peaks in which odd peaks are much more intense than even peaks are characteristic of this part of the mass scale for steroids and other carbocyclic compounds and one can readily observe even a slight increase in the intensity of the even peaks in the region where the peaks of the ion or its analogues is presumed to be.

Another characteristic of the mass spectra of steroid Δ^4-3-ketones is the presence of peaks due to the dissociation of the same 6—7 and 9—10 bonds but with fixation of the charge on the fragment containing the *C* and *D* rings. It has been shown for androst-4-en-3-one (XII) with the aid of its 8-D_1-analogue[20] that the formation of the corresponding ion j is accompanied by the migration of the hydrogen atom from $C_{(8)}$ to a neutral fragment:

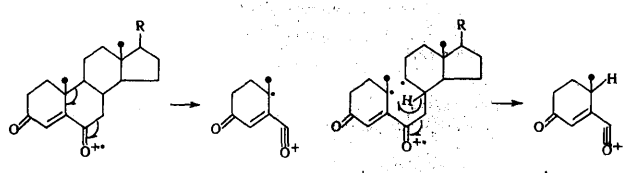


Peaks due to analogous ions have been detected also in the mass spectra of substituted progesterones[9,34]. Although this is a decomposition pathway which in general leads to low-intensity peaks and is not discussed for other Δ^4-3-ketones listed in Table 2, it is also evidently common to all Δ^4-3-ketosteroids.

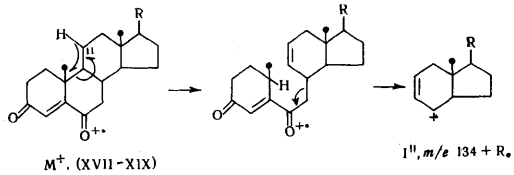
The third specific pathway in the fragmentation of Δ^4-3-ketosteroids is associated with the formation of an $(M - 42)^+$ ion (k). The probable mechanism of its formation involves the ejection of $C_{(2)}$ and $C_{(3)}$ atoms in the form of keten:



The situation changes somewhat in Δ^4-3,6-diketosteroids. Djerassi and coworkers[41] investigated the mass spectra of androst-4-ene-3,6-dione (XVII), pregn-4-ene-2,6-dione (XVIII), and cholest-4-ene-3,6-dione (XIX) and observed in them an intense double peak with *m/e* 136 and 137. The spectrum of compound (XVII) also contains an intense *m/e* 135 peak, the peaks in the triplet decreasing in the sequence 135 < 136 < 137. The peaks of the ions with *m/e* 136 (l) and 137 (l') in the mass spectrum of 2,2,7,7-D_4-(XIX) shift by 2 a.m.u., which indicates the retention of ring *A* in their structures. The involvement of the hydrogen atom at $C_{(8)}$ in the formation of the ion l' is postulated by analogy with Δ^4-3-ketones:



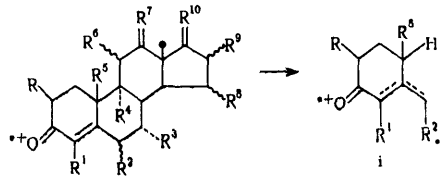
The *m/e* 135 peak (ion l''), which is characteristic of the mass spectrum of compound (XVII), shifts to *m/e* 163 and 247 in the spectra of compounds (XVIII) and (XIX) respectively. The authors suggest that the corresponding ion is formed as a result of a rearrangement involving the hydrogen atom at $C_{(7)}$ similar to the rearrangement described above for Δ^4-3-ketosteroids:



The mass spectra of the Δ^4-3,6-diketones under consideration also contain peaks of $(M - CH_2CO)^+$ ions, the formation of which may be due to both the 3-oxo-and the 6-oxo-group.

In conclusion of the section dealing with Δ^4-steroids, mention may be made also of studies on the mass-spectrometry of Δ^4-6-aza-7-ketosteroids (XX) [42,43] the spectra of which contain, despite the presence of a heteroatom in ring *B*, peaks of m, m', and m'' ions, whose intensity

Table 2. The values of *m/e* (intensity expressed as a percentage of the maximum) for the ion i in the mass spectra of Δ^4-3-ketosteroids.

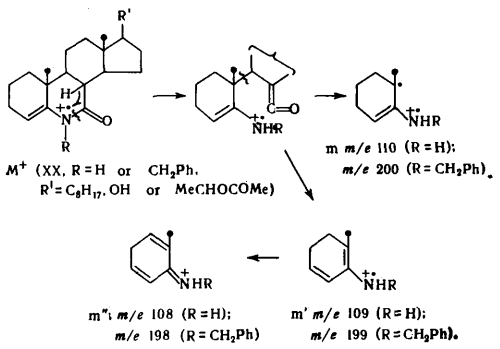


i

Compound	R	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8	R^9	R^{10}	*m/e* for ion i
Androst-4-en-3-one (XII) (Ref.20)	H	H	H	H	H	Me	H	H_2	H	H	H_2	124 (100)
17β-Hydroxyandrost-4-en-3-one (Refs.14,26)	H	H	H	H	H	Me	H	H_2	H	H	H, β-OH	124 (100)
17β-Hydroxy-10α-androst-4-en-3-one (Ref.26)	H	H	H	H	H	(α-Me)	H	H_2	H	H	H, β-OH	124 (100)
Androst-4-ene-3,17-dione (Refs.17,19)	H	H	H	H	H	Me	H	H_2	H	H	O	124 (80)
19-Norandrost-4-en-3-one (Ref.14)	H	H	H	H	H	H	H	H_2	H	H	H_2	110 (100)
19-Norandrost-4-ene-3,17-dione (Ref.27)	H	H	H	H	H	H	H	H_2	H	H	O	110 (95)
19-Nor-9β-androst-4-ene-3,17-dione (Ref.27)	H	H	H	H	(β-H)	H	H	H_2	H	H	O	110 (35)
6β-Methyl-19-norandrost-4-ene-3,17-dione (Ref.22)	H	H	β-Me	H	H	H	H	H_2	H	H	O	124 (3.4 *)
6β-Ethyl-19-norandrost-4-en-3-one (Ref.22)	H	H	β-Et	H	H	H	H	H_2	H	H	H_2	138 (1.9 *)
15α-Hydroxyandrost-4-ene-3,17-dione (Refs.28,29)	H	H	H	H	H	Me	H	H_2	α-OH	H	O	124 (40)
17α-Hydroxy-17β-methyl-19-norandrost-4-en-3-one (Ref.30)	H	H	H	H	H	H	H	H_2	H	H	α-OH, β-Me	110 (28)
17β-Hydroxy-17α-methyl-19-norandrost-4-en-3-one (Ref.30)	H	H	H	H	H	H	H	H_2	H	H	β-OH, α-Me	110 (48)
17β-Ethyl-17α-hydroxy-19-norandrost-4-en-3-one (Ref.30)	H	H	H	H	H	H	H	H_2	H	H	α-OH, β-Et	110 (30)
17α-Ethyl-17β-hydroxy-19-norandrost-4-en-3-one (Ref.30)	H	H	H	H	H	H	H	H_2	H	H	β-OH, α-Et	110 (25)
11β-Hydroxyandrost-4-ene-3,17-dione (Ref.24)	H	H	H	H	H	Me	β-OH	H_2	H	H	O	124 (60)
17α-Methyltestosterone (Ref.31)	H	H	H	H	H	Me	H	H_2	H	H	α-CH_3, β-OH	124 (40)
19-Nortestosterone (Ref.27)	H	H	H	H	H	H	H	H_2	H	H	H, β-OH	110 (100)
19-Nor-8α-testosterone (Ref.27)	H	H	H	H	H	H	H	H_2	H	H	H, β-OH	110 (25)
19-Nor-9β-testosterone (Ref.27)	H	H	H	H	(β-H)	H	H	H_2	H	H	H, β-OH	110 (100)
Progesterone (Refs.17,19,25,26,32–34)	H	H	H	H	H	Me	H	H_2	H	H	H, β-COMe	124 (100)
10α-Progesterone (Ref.26)	H	H	H	H	H	(α-Me)	H	H_2	H	H	H, β-COMe	124 (100)
17-Isoprogesterone (Ref.33)	H	H	H	H	H	Me	H	H_2	H	H	H, α-COMe	124 (25)
2α-Methylprogesterone (Ref.34)	Me	H	H	H	H	Me	H	H_2	H	H	H, β-COMe	138 (46)
4-Methylprogesterone (Ref.34)	H	Me	H	H	H	Me	H	H_2	H	H	H, β-COMe	138 (31)
6α-Methylprogesterone (Ref.34)	H	H	α-Me	H	H	Me	H	H_2	H	H	H, β-COMe	138 (100)
6β-Methylprogesterone (Ref.34)	H	H	β-Me	H	H	Me	H	H_2	H	H	H, β-COMe	138 (37)
7α-Methylprogesterone (Ref.34)	H	H	H	Me	H	Me	H	H_2	H	H	H, β-COMe	124 (21)
9α-Hydroxyprogesterone (Ref.34)	H	H	H	H	OH	Me	H	H_2	H	H	H, β-COMe	124 (84)
11-α-Hydroxyprogesterone (Refs.28,29,34)	H	H	H	H	H	Me	α-OH	H_2	H	H	H, β-COMe	124 (78)
11β-Hydroxyprogesterone (Refs.28,29,34)	H	H	H	H	H	Me	β-OH	H_2	H	H	H, β-COMe	124 (60)
Progesteron-11α-yl acetate (Ref.34)	H	H	H	H	H	Me	α-OCOMe	H_2	H	H	H, β-COMe	124 (19)
12α-Hydroxyprogesterone (Ref.35)	H	H	H	H	H	Me	H	H, α-OH	H	H	H, β-COMe	124 (20)
15α-Hydroxyprogesterone (Refs.28,29,34)	H	H	H	H	H	Me	H	H_2	α-OH	H	H, β-COMe	124 (75)
15β-Hydroxyprogesterone (Refs.28,29)	H	H	H	H	H	Me	H	H_2	β-OH	H	H, β-COMe	124 (40)
16α-Methylprogesterone (Refs.32–34)	H	H	H	H	H	Me	H	H_2	H	α-Me	H, β-COMe	124 (52)
16β-Methylprogesterone (Refs.33,34)	H	H	H	H	H	Me	H	H_2	H	β-Me	H, β-COMe	124 (43)
16β-Methyl-17-isoprogesterone (Ref.33)	H	H	H	H	H	Me	H	H_2	H	β-Me	H, α-COMe	124 (10)
16α-Hydroxyprogesterone (Refs.28,29,34)	H	H	H	H	H	Me	H	H_2	H	α-OH	H, β-COMe	124 (31)
16β-Hydroxyprogesterone (Refs.28,29)	H	H	H	H	H	Me	H	H_2	H	β-OH	H, β-COMe	124 (40)
17α-Hydroxyprogesterone (Refs.34,35)	H	H	H	H	H	Me	H	H_2	H	H	α-OH, β-COMe	124 (40)
20-Hydroxyprogesterone (Ref.35)	H	H	H	H	H	Me	H	H_2	H	H	H, β-CHOHMe	124 (100)
21-Hydroxyprogesterone (Refs.25,34)	H	H	H	H	H	Me	H	H_2	H	H	H, β-$COCH_2OH$	124 (7)
11α, 16α-Dihydroxyprogesterone (Refs.28,29)	H	H	H	H	H	Me	α-OH	H_2	H	α-OH	H, β-COMe	124 (35)
12β,15α-Dihydroxyprogesterone (Ref. 34)	H	H	H	H	H	Me	H	H, β-OH	α-OH	H	H, β-COMe	124 (43)
6α,16α-Dimethylprogesterone (Refs.22,32)	H	H	α-Me	H	H	Me	H	H_2	H	α-CH_3	H, β-COMe	138 (7.4*)
6α,16β-Dimethylprogesterone (Ref.32)	H	H	α-Me	H	H	Me	H	H_2	H	β-CH_3	H, β-COMe	138 (100)
17α-Hydroxy-16α-Methylprogesterone (Ref.32)	H	H	H	H	H	Me	H	H_2	H	α-CH_3	α-OH, β-COMe	124 (47)
16α,17α-Dimethylprogesterone (Ref.36)	H	H	H	H	H	Me	H	H_2	H	α-Me	α-CH_3, β-COMe	124 (8)
17α-Hydroxy-6β,16α-Dimethylprogesterone (Ref.32)	H	H	β-Me	H	H	Me	H	H_2	H	α-Me	α-OH, β-COMe	138 (53)
Cortisol (Refs.24,25)	H	H	H	H	H	Me	β-OH	H_2	H	H	α-OH, β-$COCH_2OH$	124 (40)
Corticosterone (Ref.25)	H	OH	H	H	H	Me	β-OH	H_2	H	H	H, β-$COCH_2OH$	124 (20)
Cholest-4-en-3-one (XIII) (Refs.14,17,19)	H	H	H	H	H	Me	H	H_2	H	H	H, β-C_8H_{17}	124 (100)
4-Hydroxycholest-4-en-3-one (Ref.22)	H	H	H	H	H	Me	H	H_2	H	H	H, β-C_8H_{17}	140 (2.7*)
6β-Methylcholest-4-en-3-one (Ref.18)	H	H	β-Me	H	H	Me	H	H_2	H	H	H, β-C_8H_{17}	138 (100)
19-Hydroxycholest-4-en-3-one (Ref.35)	H	H	H	H	H	CH_2OH	H	H_2	H	H	H, β-C_8H_{17}	110 (20)
24-Hydroxycholest-4-en-3-one (Ref.35)	H	H	H	H	H	Me	H	H_2	H	H	H, β-$C_8H_{16}OH$	124 (100)
25-Hydroxycholest-4-en-3-one (Ref.35)	H	H	H	H	H	Me	H	H_2	H	H	H, β-$C_8H_{16}OH$	124 (100)
26-Hydroxycholest-4-en-3-one (Refs.35,37)	H	H	H	H	H	Me	H	H_2	H	H	H, β-$C_8H_{16}OH$	124 (100)
3-Oxocholest-4-en-26-yl acetate (Ref.37)	H	H	H	H	H	Me	H	H_2	H	H	H, β-$C_8H_{16}OCOMe$	124 (100)
Methyl 3-oxocholest-4-en--26-oate (Ref.37)	H	H	H	H	H	Me	H	H_2	H	H	H, β-$C_7H_{14}COOMe$	124 (100)
Methyl 7α,12α-Dihydroxy-3-oxochol--4-enoate (Ref.38)	H	H	H	α-OH	H	Me	H	H, α-OH	H	H	H, β-C_4H_8COOMe	124 (100)
Methyl 7α,12α-Dihydroxy-3-oxobisnorchol--4-enoate (Ref.38)	H	H	H	α-OH	H	Me	H	H, α-OH	H	H	H, β-C_2H_4COOMe	124 (100)
Methyl 7α-hydroxy-3,12-dioxochol-4--enoate (Ref.39)	H	H	H	α-OH	H	Me	H	O	H	H	H, β-C_4H_8COOMe	124 (25)
Methyl 7α-hydroxy-3,12-dioxobisnorchol-4--enoate (Ref.39)	H	H	H	α-OH	H	Me	H	O	H	H	H, β-C_2H_4COOMe	124 (90)

* Intensity expressed as a percentage of the total ionic current.

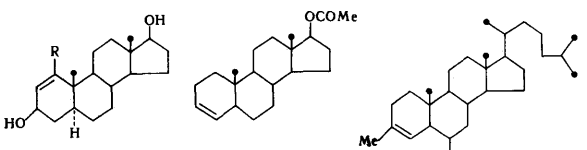
is highest, which are also due to the dissociation of the 6—7 and 9—10 bonds:



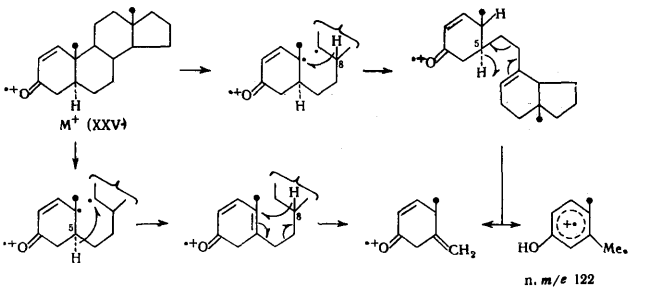
3. Δ^1- and Δ^3-Steroids

Specific fragmentation pathways have not been observed in Δ^1- and Δ^3-steroids without functional groups near the double bond. Thus the most intense peak in the mass spectrum of 1-methyl-5α-androst-1-ene-3β,17β-diol (XXI) [7] is that with *m/e* 220, the structure of the corresponding ion being most probably similar to that of the ion a. Probably the fragmentation of the molecular ion of compound (XXI) resembles the decomposition of Δ^2-steroids, which hinders their identification. Spitteller and coworkers[8,9] noted that fragments typical of Δ^4-steroids can be detected in the spectrum of compound (XXII), the 1-desmethyl analogue of compound (XXI).

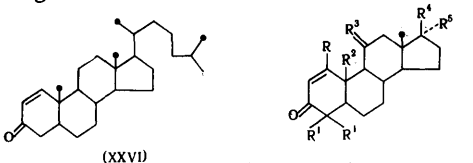
One of the main peaks in the spectrum of androst-3-en-17β-yl acetate (XXIII) [9] is one with *m/e* 108 (ion h, $C_8H_{12}^+$), which is also characteristic of 4-cholestene (VIII). In the spectrum of 3-methylcholest-3-en-6β-yl acetate (XXIV), [18] there is no molecular ion peak, the dominant intensity being that of the peak due to the $(M - CH_3COOH)^+$ ion, which corresponds to the maximum mass number. The latter subsequently splits off part of ring *A* with formation of an $(M - 60 - 68)^+$ ion corresponding to *m/e* 314; its formation is a result of the RDR ejection of an isoprene molecule (68 a.m.u.), which is more likely to be typical for the corresponding Δ^2-steroid:



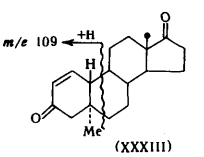
The mass spectra of Δ^1-3-ketosteroids are significantly more characteristic. The decomposition of these compounds resembles that of their Δ^4-3-keto-isomers. The most intense peak in the mass-spectrum of 5α-androst-1-en-3-one (XXV) [20] is that of the *m/e* 122 ion n. Judging from its mass number, this ion should form as a result of a simple dissociation of the 6—7 and 9—10 bonds without the migration of a hydrogen atom. However, analysis of the mass spectra of the 5α- and 8β-D_1 analogues of compound (XXV) showed that in the formation of the ion n hydrogen atoms move towards each other, that from $C_{(5)}$ migrating to the neutral fragment and that from $C_{(8)}$ to the charged fragment. The following possible mechanism for the formation of the ion n has been proposed on the basis of these results[20,21]:



Intense peaks due to the ions n (*m/e* 122) are present also in the mass spectra of cholest-1-en-3-one (XXVI), [22] 5α-androst-1-ene-3,11-dione (XXVII), 17β-hydroxy-5α(and 5β)-androst-1-en-3-ones (XXVIII), and 5α(and 5β)-androst-1-ene-3,17-diones (XXIX) [44] and the peaks of the homologous ions with *m/e* 136, 150, and 108 are present in the spectra of 17β-hydroxy-1-methyl-5α-androst-1-ene-3-one (XXX), 4,4-dimethyl-5α-cholest-1-en-3-one (XXXI), [22] and 19-nor-Δ^1-3-ketosteroids (XXXIIa, b) respectively. In connection with the different behaviour of Δ^1- and Δ^4-3-ketosteroids, it has been suggested[14] that the reason why the ion n cannot be formed from the latter is the absence of a hydrogen atom at $C_{(5)}$, which is necessary for the migration of the two hydrogen atoms towards one another described above. This hypothesis is confirmed by the finding that the mass spectrum of 5α-methyl-19-norandrost-1-ene-3,17-dione (XXXIII), [18] which also lacks a hydrogen atom at $C_{(5)}$, contains virtually no peak with *m/e* 122, the main peak being one with *m/e* 109, which probably arises on dissociation of the 5—6 and 9—10 bonds with migration of a hydrogen atom to the charged fragment.



(XXVII, R = R1 = R4 = R5 = H, R2 = Me, R3 = O);
(XXVIII, R = R1 = R5 = H, R2 = Me, R3 = H2, R4 = OH, 5α- and 5β-);
(XXIX, R = R1 = H, R2 = Me, R3 = H2, R4 + R5 = O);
(XXX, R = R2 = Me, R1 = R5 = H, R3 = H2, R4 = OH);
(XXXI, R = R5 = H, R1 = R2 = Me, R3 = H2, R4 = C8H17);
(XXXIIa, R = R1 = R2 = R5 = H, R3 = H2, R4 = OCOMe, 5α- and 5β-);
(XXXIIб, R = R1 = R2 = H, R3 = H2, R4 = COMe R5 = OH).



Thus, in contrast to Δ^4-3-ketosteroids, the dissociation of the 6—7 and 9—10 bonds in Δ^1-3-ketosteroids is accompanied only by the migration of hydrogen atoms towards one another and the corresponding characteristic peak of the ion n is smaller by 2 a.m.u. than the peak of the ion i, which is characteristic of Δ^4-3-ketosteroids.

It is striking that the intensity of the peak due to the ion n depends on the configuration at $C_{(5)}$ and is always greater in the 5β-series[44,45].

The presence in the Δ^1-3-ketosteroid molecule of an $\alpha\beta$-unsaturated keto-chromophore is the reason for the elimination of keten from M^+. This process has been noted for the majority of the Δ^1-3-ketones described above and in this respect their decomposition is analogous to that of their Δ^4-3-keto-isomers, which leads to ions of type k. Egger[44] suggested that the absence of the peak of the $(M - 42)^+$ ion from the mass spectrum of the 5β-isomer (XXVIII) be employed to determine the configuration of the

5th centre in steroids of the Δ^1-3-keto-series. However, Schulz[45] did not find a similar difference in the 5α- and 5β-Δ^1-3-ketones which he investigated, and noted the presence of the peak of the $(M - 42)^+$ ion in the spectra of the 5α- and 5β-isomers of compound (XXXIIa) and its absence from the spectra of the 5α- and 5β-isomers of compound (XXXIIb).

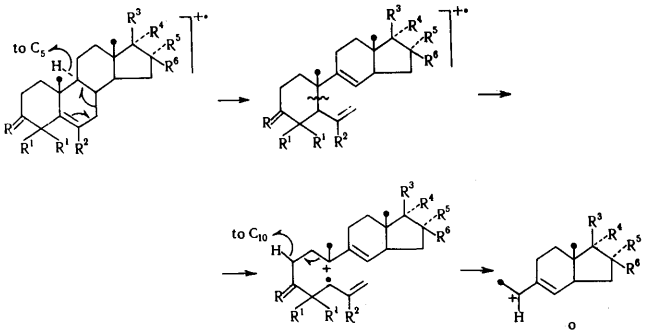
III. STEROIDS WITH A DOUBLE BOND IN RING *B*

1. Δ^5-Steroids

A large number of natural steroids, particularly of plant origin, contain a double bond in the 5—6 position. A combined gas—liquid chromatographic and mass-spectrometric method has been widely used recently to investigate natural steroid mixtures. As a rule, volatile steroid derivatives—acetates and especially trimethylsilyl ethers—are used in such investigations. In many studies of this kind, no data were obtained whereby one could infer the influence of the position of the double bond on the nature of the decomposition of the molecular ion under electron impact. Naturally, these investigations are not considered here.

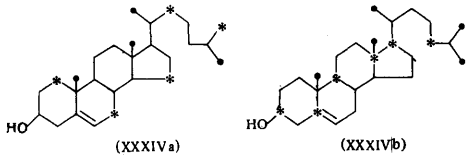
In one of the first mass-spectrometric studies on Δ^5-steroids, Friedland et al.[46] were the first to draw attention to the intense peak due to ions with *m/e* 275, 303, and 177, among the many peaks characteristic of the majority of steroids, in the spectra of cholesterol (XXXIV), β-sitosterol (XXXV), and dehydroepiandrosterone (XXXVI) respectively. They attributed the formation of these ions to the dissociation of the 9—10 bond and of the 5—6 vinylic bond. Somewhat later Ryhage and Stenhagen[15] also published the spectrum of cholesterol but failed to interpret many of the peaks in it, including the *m/e* 275 peak. We undertook a systematic study of the effect of the Δ^5-bond [17,19] in numerous Δ^5-3-hydroxy- and Δ^5-3-keto-steroids. Regardless of the conditions employed during its recording (a heated glass filling system or direct introduction into the ion source), the mass spectrum of cholesterol (XXXIV) shows an intense *m/e* 275 peak, the intensity of which depends on that of the peak due to the molecular ion: in experiments with a hot glass inlet system at 200°C, the intensity of the *m/e* 275 peak decreases together with decrease of that of the molecular ion peak; under milder conditions, when the specimen is introduced directly into the ion source, the size of the *m/e* 275 peak differs little from the molecular ion peak, which predominates in the spectrum.

The mass spectrum of cholest-5-en-3-one (XXXVII),[17,19] recorded on an apparatus with a heated glass filling system at 200°C, is identical with the spectrum of cholest-4-en-3-one (XIII), which indicates the ease of the thermal isomerisation of Δ^5-3-ketones under the conditions of mass-spectrometric measurements. However, when the apparatus with direct introduction of the specimen into the ion source is employed, the mass spectrum of compound (XXXVII) differs significantly from that of compound (XIII), since it contains an intense *m/e* 275 peak (ion o). The *m/e* 275 peak of the ion o is observed also in the spectrum of cholest-5-ene (XXXVIII).[8,9,17] Similarly the spectra of pregn-5-en-3,20-dione (XXXIX) and androst-5-ene-3,17-dione (XL) show intense peaks with *m/e* 205 and 177 respectively, which are absent from the spectra of the isomeric Δ^4-3-ketones. However, it is noteworthy that the spectra of the Δ^5-3-ketones as a rule also show peaks with *m/e* 124 (ion i) and M − 42, which are characteristic of Δ^4-3-ketones. This indicates a partial isomerisation of Δ^5-3-ketones to Δ^4-3-ketones even under mild experimental conditions. Thus one may conclude that the ions o are characteristic of Δ^5-steroids. Since the mass number of the ion o depends on the size of the side chain at $C_{(17)}$, it must contain rings *C* and *D* together with the side chain (Table 3). In view of the fact that the mass number of the ion o does not vary with substitution in ring *A*, the latter must be absent (or only a small portion of it remains at the junction with ring *B*). On the other hand, the $C_{(6)}$ atom does not enter into the composition of the ion o, since in the spectrum of 6-methylcholesterol (XLI) [18,19] its mass number remains unchanged compared with the spectrum of compound (XXXIV). Thus the mechanism of the formation of the *m/e* 275 ion, proposed previously[46], is erroneous and the following mechanism may be proposed for the formation of the ion o:[8,18]



The mechanism shows that the ion o is probably formed directly from the molecular ion, although the corresponding metastable peak was not observed. This hypothesis is confirmed indirectly by the fact that in the spectra of compounds which do not contain the peak of the molecular ion, or its intensity is low, the intensity of the peak due to the ion o is greatly reduced, sometimes to such an extent that it cannot be reliably identified. For example, in the spectra of the acetate (XLII), trifluoroacetate (XLIII), and trimethylsilyl ether of cholesterol (XLIV), of which the first two altogether fail to give rise to the molecular ion peak and the third contains a low-intensity M^+ peak, the peaks of the ion o are small (Table 3).

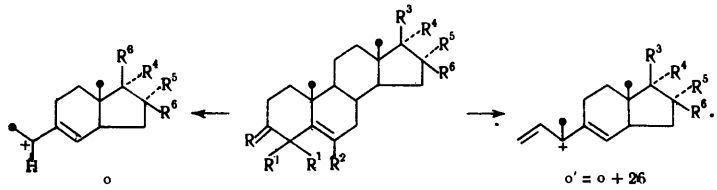
The final proof of the origin of the ion o can be obtained by studying the spectra of labelled compounds. In this connection, Knights[47] put forward an interesting idea. He suggested that one should investigate the mass spectra of cholesterols labelled with ^{13}C in various positions of the steroid skeleton, namely the spectra of compounds (XXXIVa) and (XXXIVb), which may be obtained by biosynthesis from [2-^{13}C]- and [4-^{13}C]-mevalonic acids respectively. However, this has not been achieved experimentally.



(XXXIVa) (XXXIVb)

The mass spectra of Δ^5-3-hydroxysteroids contain, together with peaks of the ions o, peaks with an intensity higher by 26 a.m.u. (o + 26, ion o′), which are not observed in the spectra of Δ^5-3-ketones (Table 3). As a rule, the intensity of these peaks is of the same order of

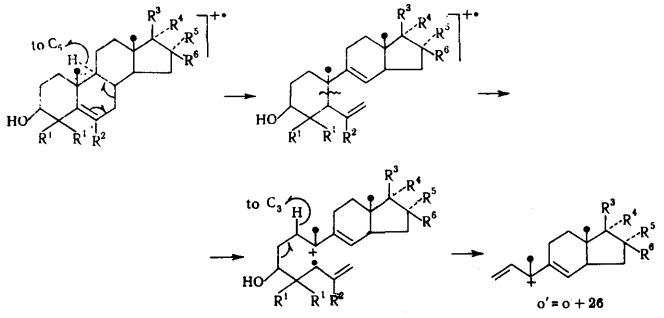
Table 3. The values of *m/e* (intensity expressed as a percentage of the M^+ peak) for the ions o and o′ in the mass spectra of Δ^5-steroids.



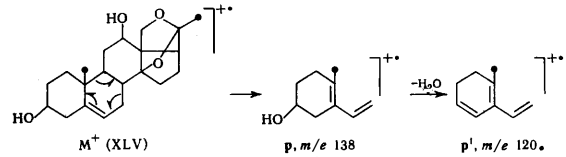
Compound	R	R^1	R^2	R^3	R^4	R^5	R^6	*m/e* for ion o	*m/e* for ion o′
Cholest-5-ene (XXXVIII) (Refs.8,17)	H_2	H	H	C_8H_{17}	H	H	H	275 (22)	301 (25)
Cholesterol (XXXIV) (Refs.17,19,46,47)	H, β-OH	H	H	C_8H_{17}	H	H	H	275 (90)	301 (45)
Cholest-5-en-3-one (XXXVII) (Refs.17,19)	O	H	H	C_8H_{17}	H	H	H	275 (12)	—
Pregn-5-ene-3,20-dione (XXXIX) (Refs.17,19)	O	H	H	$COCH_3$	H	H	H	205 (17)	—
Androst-5-ene-3,17-dione (XI) (Refs.17,19)	O	H	H	$R^3+R^4=O$		H	H	177 (30)	—
β-Sitosterol (XXXV) (Refs.17,46,47)	H, β-OH	H	H	$C_{10}H_{21}$	H	H	H	303 (70)	329 (40)
Stigmasterol (Ref.17)	H, β-OH	H	H	$C_{10}H_{19}$	H	H	H	301 (18)	—
Campesterol (Ref.47)	H, β-OH	H	H	C_9H_{19}	H	H	H	289 (65)	315 (60)
16α,17α-Epoxy-3β-hydroxypregn-5-en-20-one (Ref.17)	H, β-OH	H	H	$COCH_3$	$R^4+R^5=O$		H	219 (16)	345 (20)
4,4-Dimethylcholesterol (Ref.17)	H, β-OH	CH_3	H	C_8H_{17}	H	H	H	275 (8)	205 (5)
4,4-Dimethylcholest-5-en-3-one (Ref.17)	O	CH_3	H	C_8H_{17}	H	H	H	275 (8)	—
6-Methylcholesterol (XLI) (Refs.18,19)	H, β-OH	H	CH_3	C_8H_{17}	H	H	H	275 (25)	—
17β-Hydroxyandrost-5-en-3-one (Ref.17)	O	H	H	OH	H	H	H	179 (30)	—
Androst-5-ene-3β,17β-diol (Ref.17)	H, β-OH	H	H	OH	H	H	H	179 (53)	205 (50)
13-Isoandrost-5-ene-3β,17β-diol (Refs.48,49)	H, β-OH	H	H	OH	H	H	H	179 (40)	205 (20)
13-Isoandrost-5-ene-3β,17α-diol (Refs.48,49)	H, β-OH	H	H	H	OH	H	H	179 (35)	205 (18)
Dehydroepiandrosterone (XXXVI) (Ref.46)	H, β-OH	H	H	$R^3+R^4=O$		H	H	177 (63)	203 (60)
3β-Hydroxyandrost-5-en-16-one (Ref.18)	H, β-OH	H	H	H	H	$R^5+R^6=O$		177 (28)	—
Cholesteryl acetate (XLII) (Ref.47)	H, β-OAc	H	H	C_8H_{17}	H	H	H	275 (4 *)	—
Cholesteryl trifluoroacetate (XLIII) (Ref.47)	H, β-OCCOF$_3$	H	H	C_8H_{17}	H	H	H	275 (6 *)	—
Trimethylsilyl ether of cholesterol (XLIV) (Refs.47,50)	H,β-OSiMe$_3$	H	H	C_8H_{17}	H	H	H	275 (8 *)	301 (4 *)
Trimethylsilyl ether of β-sitosterol (Ref.50)	H,β-OSiMe$_3$	H	H	$C_{10}H_{21}$	H	H	H	303 (10 *)	329 (8 *)
Trimethylsilyl ether of campesterol (Ref.50)	H,β-OSiMe$_3$	H	H	C_9H_{19}	H	H	H	289 (10 *)	315 (8 *)

* Intensity expressed as a percentage of the maximum in the spectrum.

magnitude as that of peaks due to the ions o. The data in Table 3 lead to the conclusion that the ions o′ contain rings *C* and *D* and do not contain the $C_{(4)}$ atom. However, they also incorporate the $C_{(1)}$ and $C_{(2)}$ atoms. A formal mechanism has been proposed for the formation of both the o and o′ ions assuming the retention in the latter of the most probable carbon atoms[8,18]:

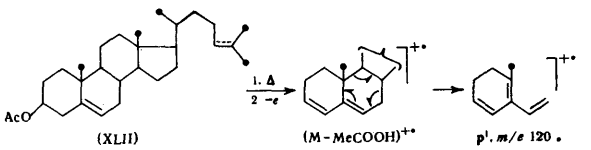


In principle one may expect that Δ^5-steroids should decompose via a type RDR mechanism. One cannot rule out the possibility that in the cases described above this process does occur but only to such a slight extent that the corresponding peaks are difficult to observe against the background of the surrounding peaks. This applies particularly to the peaks of the diene fragments, since their mass numbers are usually smaller than 100 and this region contains fairly intense uncharacteristic peaks typical for all carbocyclic compounds. Nevertheless in the case of certain Δ^5-steroids containing labile functional groups, the spectra of which show low-intensity peaks due to molecular ions (this precludes an unambiguous identification of the peaks due to the ions o and o′), peaks caused by RDR in ring *B* frequently appear. Reichstein and coworkers[51] observed in the spectrum of stapelogenin (XLV) a medium-intensity *m/e* 138 peak (ion p) due to a type RDR decomposition. This ion is accompanied by one formed as a result of dehydration (the ion p′). The origin of the ions has been confirmed by comparison with the spectrum of the di-OD-analogue of compound (XLV):



Later Galli and Maroni[52] observed *m/e* 120 peaks of the ion p′ in the mass spectra of cholesteryl acetate (XLII) and cholesta-5,24-dien-3β-yl acetate (XLVI) (with intensities of 30 and 15% respectively), which arise as a result of RDR in the $(M - CH_3COOH)^+$ ion. Probably the latter is formed by the thermal elimination of CH_3COOH, since these spectra do not contain M^+ peaks and the peaks

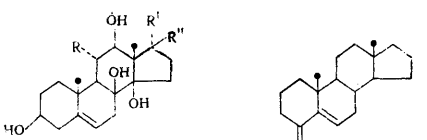
of the $(M - CH_3COOH)^+$ ions have the highest mass number.



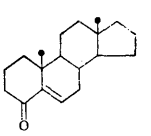
(XLII) (XLVI. Δ^{24})

The mass spectra of compounds (XLII) and (XLVI) contain also the peaks of *m/e* 247 and 245 ions, which are probably formed on dissociation of the same bonds (7—8 and 9—10) but with migration of hydrogen and location of the charge on the dienophile fragment.

In a recent mass-spectrometric study of a large number of polyols of the 5-pregnene series, of the type of marsdenin (XLVII) and sarcostin (XLIII), Fukuoka et al.[53] also observed peaks of ions p and p'. They likewise interpreted a series of other peaks produced by a mechanism similar to that of the formation of the ions p and p' but involving a rearrangement of the hydrogen atoms. The presence of peaks due to ions formed by the dissociation of the same bonds (7—8 and 9—10), but involving the fixation of the charge on the dienophile fragment with $m/e = M^+ - 138$ ($M^+ - 180$ for 3-acetoxy-derivatives), was noted in the same investigation.



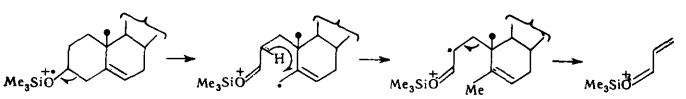
(XLVII, R=OH, R'=COMe, R''=H);
(XLVIII, R=H, R'=CHOHMe, R''=OH)



(XLIX).

Thus the peaks of the ions p and p' or o and o' are diagnostic in the series of Δ^5-steroids, depending on the stability of the molecular ion and the presence of labile functional groups. It is interesting to note that the mass spectrum of androst-5-en-4-one (XLIX) [54] also contains the peaks of the ion o with *m/e* 163. Von Unruh and Spiteller[55] believe that the peaks of *m/e* 135, 147, and 149 ions are characteristic of compound (XLIX). The first two probably arise in a type RDR decomposition in ring *B* with migration of the hydrogen atom to or away from the charged fragment; it is not clear which half of the molecule is charged under these conditions.

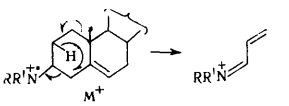
Certain data concerning the capacity of trimethylsilyl ethers of Δ^5-3-hydroxysteroids to give rise to ions of types o and o' in decomposition under electron impact are presented in Table 3. Another characteristic of the decomposition of these derivatives is the ease of formation of the ion with *m/e* 129 (r) whose peak is the most intense in their spectra[50,56-58] (in the spectra of the corresponding saturated analogues, the peak of this ion is insignificant). The ease of formation of the ion r on decomposition of Δ^5-steroids is due to the dissociation of two allylic bonds (3—4 and 1—10), which is confirmed by their comparison with the spectra of deutero-analogues[57]:



r, *m/e* 129

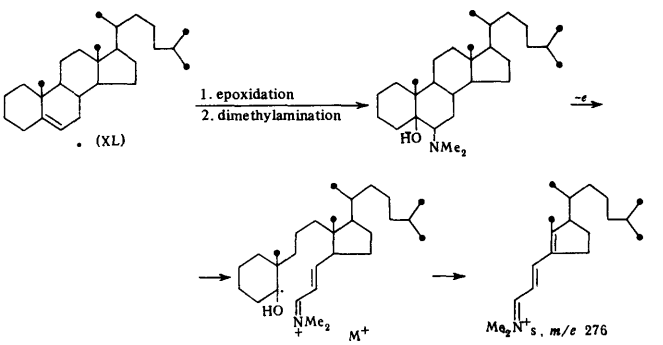
It is noteworthy that the presence of the Δ^5-bond greatly intensifies the elimination of $(CH_3)_3SiOH$ from the molecular ion[57,58], which in all probability results in the formation of the ion of the conjugated 3,5-diene.

In a manner similar to the increase of the intensity of the peak of the ion r on passing from saturated to Δ^5-3-trimethylsilyloxy-derivatives, there is a sharp increase of the intensity of the peak due to the ion r' in the mass spectra of 3-amino-Δ^5-steroids compared with their saturated analogues[59-65]. The mechanism of the formation of the ion r' is evidently similar to that of the formation of the ion r, the dissociation of two allylic bonds (3—4 and 1—10), which intensifies the formation of the ion r', also being responsible for the occurrence of this process:



r', (R=R'=H), *m/e* 56;
(R=H, R'=Me), *m/e* 70;
(R=R'=Me), *m/e* 84;.

In conclusion of the discussion of Δ^5-steroids, attention should be drawn to the interesting method of determining the position of the double bond in these compounds, proposed by Reed[66]. Although the principle of this method has been demonstrated only for 5-cholestene (XL), it is presumably of more general validity. Its essential feature is that the test compound is epoxidised, the epoxide treated with dimethylamine, and the resulting α-aminoalcohol analysed mass-spectrometrically. The presence in the mass spectrum of the peak due to the ion s serves as evidence of the presence of a Δ^5-bond in the olefin investigated:

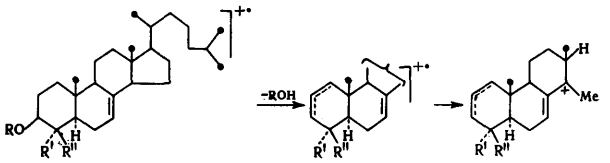


(XL)

2. Δ^7-Steroids

Compounds containing the double bond in the 7—8 position occupy an important place among plant sterols. A number of mass-spectrometric studies have been made on hydroxysteroids of this type, particularly their ethers, trimethylsilyl ethers, and acetates. Gustavsson et al.[58], who considered the mass spectra of the trimethylsilyl ethers of 5α-cholest-7-en-3β-ol (L) and 4α-methyl-5α-cholest-7-en-3β-ol (LI), noted the insignificant intensity of the peaks of the ions r. In addition, they pointed out the presence in the spectra of these compounds of peaks due to ions with *m/e* 229 and 243, the nature of which they failed to establish. Galli and Maroni[52] also observed peaks due to ions with *m/e* 229, 243, and 257 in 5α-cholest-7-en-3β-yl (LII), 4α-methyl-5α-cholest-7-en-3β-yl (LIII), and 4,4-dimethyl-5α-cholest-7-en-3β-yl (LIV) acetates respectively. Having investigated a large number of acetate and trifluoroacetate esters and trimethylsilyl ethers of Δ^7-3-hydroxysteroids, Knights[47] concluded that the formation of the ions t as a result of the elimination of the substituents at $C_{(3)}$ together with a hydrogen atom from the side chain and part of ring *D* is most characteristic of these compounds.

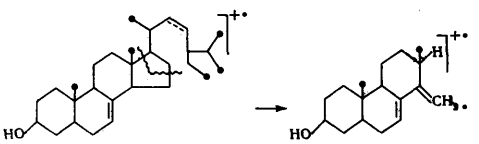
The formation of the ion t can be represented in a general form as follows:



M^+, (L, R = Me_3Si, R' = R'' = H);
(LI, R = Me_3Si, R' = Me, R'' = H);
(LII, R = COMe, R' = R'' = H);
(LIII, R = COMe, R' = Me, R'' = H);
(LIV, R = COMe, R' = R'' = Me)

t, (R' = R'' = H), *m/e* 229;
(R' = Me, R'' = H), *m/e* 243;
(R' = R'' = Me), *m/e* 257.

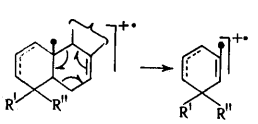
In a study of the mass spectra of stigmast-7-en-3β-ol (LV) and stigmasta-7,22-dien-3β-ol (LVI), Clark-Lewis and Dainis[67] drew attention to the *m/e* 246 fragment (t') which they also regard as characteristic of Δ^7-steroids:



M^+ (LV)
(LVI: Δ^{22})

t, *m/e* 246

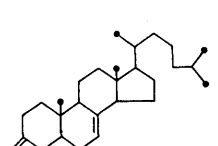
Without denying that the formation of the ions p is characteristic of the decomposition of Δ^7-steroids under electron impact, Galli and Maroni[52] nevertheless believe that type RDR decomposition in ring *B* is more important. They detected peaks with *m/e* 94, 108, and 122 (the ions u) in the mass spectra of compounds (LII), (LIII), and (LIV) respectively, which are probably formed as a result of RDR after the elimination of the functional group at $C_{(3)}$ with an additional hydrogen atom:



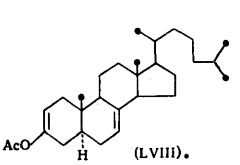
$(M-ROH)^{+\cdot}$ (LII-LIV)

u, (R' = R'' = H), *m/e* 94;
(R' = Me, R'' = H), *m/e* 108;
(R' = R'' = Me), *m/e* 122.

We believe that the ion u is difficult to employ for the identification of the Δ^7-bond, since the spectra of all steroids contain groups of peaks of approximately equal intensity with *m/e* 91—96, 105—110, and 119—124 against the background of which it is not always possible to isolate the required peak with certainty. Moreover, the process cannot be regarded in principle as specific to the steroid olefins under consideration. For example, in the spectrum of cholest-7-en-3-one (LVII) [18] there is no peak corresponding to the ion u, but there are peaks due to ions of types t and t' (both contain the C=O group). In 5α-cholesta-2,7-dien-3β-yl acetate (LVIII),[68] RDR in ring *B* is not observed either but the peak due to the fragment caused by type RDR decomposition in ring *A*, characteristic of Δ^2-steroids, is very intense (75% of the maximum peak in the spectrum).



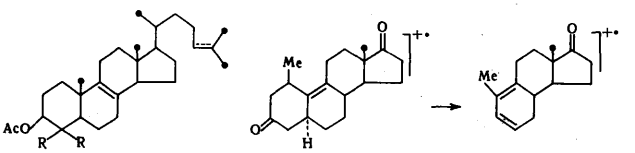
(LVII)



(LVIII).

3. Δ^8- and Δ^9-Steroids

In a study of the mass spectra of cholesta-8,24-dien-3β-yl (LIX), cholest-8-en-3β-yl (LX), and 4,4-dimethylcholest-8-en-3β-yl (LXI) acetates, Galli and Maroni[52] failed to observe the peaks of characteristic ions the formation of which might have been due to the Δ^8-bond.



(LIX, R = H, Δ^{24});
(LX, R = H);
(LXI, R = Me)

M^+ (LXII)

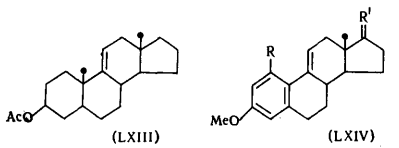
v, *m/e* 216.

The mass spectrum of 1β-methyl-19-norandrost-9-en-3,17-dione (LXII) [18] is fairly characteristic, but on the basis of this single example it is hardly possible to conclude that the decomposition pathways considered are typical for all Δ^9-steroids. After the molecular ion peak, the most intense peak in the spectrum of compound (LXII) is that of the ion with *m/e* 216 (v), which is most probably formed as a result of the ejection of the 1-CH_3 group and the cyclopropanone moiety (atoms $C_{(2)}$ – $C_{(4)}$) from ring *A*, although one cannot rule out the possibility that this ion can be formed from the $(M-15)^+$ ion with scission of part of ring *D* (atoms $C_{(15)}$ – $C_{(17)}$).

IV. STEROIDS WITH A DOUBLE BOND IN RING *C*

1. $\Delta^{9(11)}$-Steroids

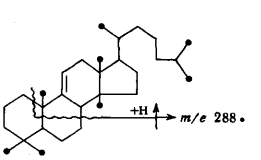
Despite the fact that the double bond in the 9—11 position might initiate type RDR decomposition, the mass spectra of androst-9(11)-en-3β-ol (LXIII) and derivatives of $\Delta^{9(11)}$-dehydro-oestrone (LXIV, a—c) [3,69] do not contain the corresponding peaks:



(LXIII) (LXIV)

(a, R = H, R' = H, OH);
(b, R = OMe, R' = O);
(c, R = Me, R' = O)

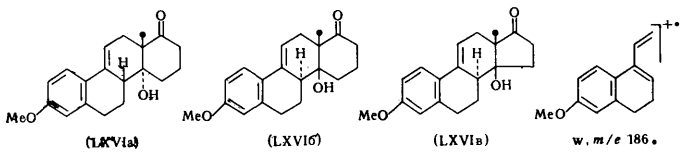
This is in full agreement with Reed's observation[11] that the peak of the *m/e* 204 ion (produced as a result of a type RDR decomposition) has only a slight intensity in the spectrum of lanost-9(11)-ene, while the peak of the $(M-15)^+$ ion (evidently produced by the ejection of the 19-CH_3 group) and the peak of the *m/e* 288 ion formed as a result of the dissociation of three allylic bonds (1—10, 5—10, and 7—8) with transfer of a hydrogen atom to the charged fragment, are very intense:



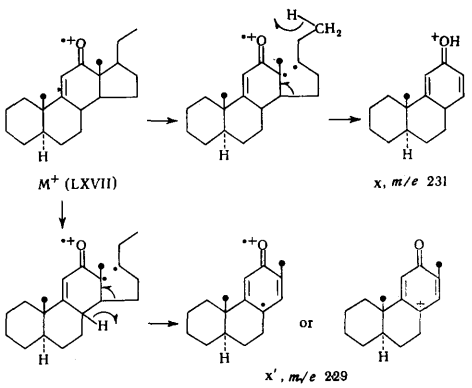
(LXV)

In contrast, in the mass spectra of the methyl ethers of $\Delta^{9(11)}$-dehydro-14α-hydroxy-D-homo-oestrone (LXVIa), $\Delta^{9(11)}$-14β-hydroxy-8α-D-homoiso-oestrone (LXVIb), and $\Delta^{9(11)}$-dehydro-14β-hydroxy-8α-iso-oestrone (LXVIc) the dominant peaks correspond to ions with *m/e* 186 (w).[70,71]

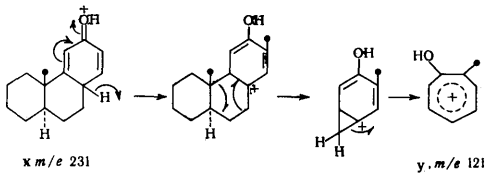
Although medium-intensity peaks with the same value of m/e are present in the mass spectra of almost all oestrone derivatives without the 9—11 double bond, their sharp increase in the spectra of compounds (LXVI, a—c) is apparently evidence that in this case the ions w are formed via a type RDR mechanism:



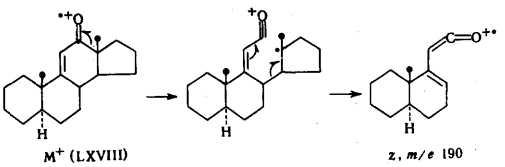
Tökes and Djerassi[72] made a mass-spectrometric study of $\Delta^{9(11)}$-12-keto-steroids and found that the mass spectrum of 5α-pregn-9(11)-en-12-one (LXVII) contains, together with the intense m/e 231 peak (the ion x), due to the elimination of ring D and the migration of a hydrogen atom to the charged moiety (the composition typical for 12-ketosteroids), there is also a peak due to an ion with m/e 229 (x′) formed as a result of an analogous process with migration of a hydrogen atom from the 8β-position in the charged species:



The maximum peak in the spectrum of compound (LXVII) with m/e 121 (the ion y) is due to further decomposition of the ion x:



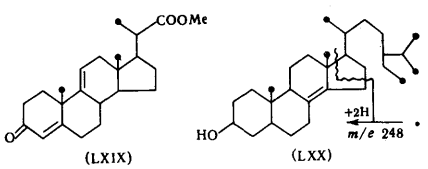
In contrast to compound (LXVII), in the mass spectrum of 5α-androst-9(11)-en-12-one (LXVIII) there are virtually no peaks due to the ions x and y. It was also suggested[72] that this is due to the absence from compound (LXVIII) of a substituent at $C_{(17)}$, which initiates the dissociation of the 13—17 bond and serves as a donor of a hydrogen atom from the 20-position in the course of the formation of the ion x. The peak of the m/e 147 ion ($C_{10}H_{11}O^+$), which contains, according to the mass-spectrometric data for the 8,11-dideutero-analogue of compound (LXVIII), the $C_{(8)}$ and $C_{(11)}$ atoms, predominates in the spectrum of compound (LXVIII). Moreover, the spectrum of this compound contains a medium-intensity peak due to an ion with m/e 190 (z) caused by the dissociation of the 8—14 and 12—13 bonds. In compound (LXVII) this process is less characteristic:



Ions of types x, y, and z are also present in the mass spectrum of the ester of 3,12-dioxobisnorchola-4,9(11)-dienoic acid (LXIX).[18]

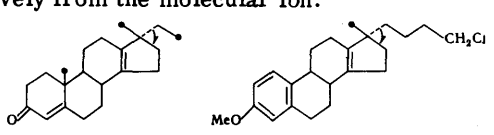
2. $\Delta^{8(14)}$-Steroids

The mass spectra of only two examples of compounds of this type have been described, namely of stigmast-8(14)-enol (LXX) and its acetate. Clark-Lewis and Dainis[57] believe that the peaks of ions with m/e 248 and 234, are characteristic of both compounds; the first is evidently formed as a result of the dissociation of the 13—17 and 15—16 bonds accompanied by the migration of two hydrogen atoms to the charged fragment. Naturally this one example is insufficient to assess whether or not this process is characteristic of all $\Delta^{8(14)}$-steroids.



V. STEROIDS WITH A DOUBLE BOND IN RING D

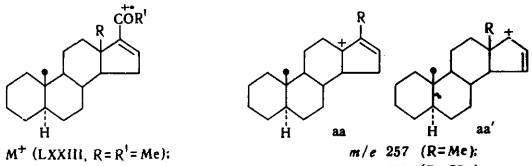
The presence of a double bond in the 13—14 position in the steroid molecule stimulates the dissociation of the allylic 17—20 bond with elimination of the substituent at $C_{(17)}$ and therefore the mass spectra of 17α-ethyl-17β-methyl-18-norandrosta-4,13-dien-3-one (LXXI) and 17α-(γ-chloropropyl)-3-methoxy-17β-methyl-18-norоestra-1,3,5(10),13-tetraene (LXXII) show[73] very intense peaks associated with the elimination of C_2H_5 and C_3H_6Cl respectively from the molecular ion:



Peterson[32] quotes mass-spectrometric data for a group of Δ^{16}-steroids of the pregnane series, a characteristic feature of which is the absence of peaks due to the elimination of ring D from the molecular ion with formation of the so called "tricyclic fragment" containing rings A, B, and C. Generally speaking, this process should be inhibited in all compounds containing a double bond in any position in ring D, since its occurrence requires the dissociation of at least one double bond.

Tökes and Djerassi[72] confirmed the absence of the peak due to the "tricyclic fragment" from the spectrum of 5α-pregn-16-en-20-one (LXXIII) and noted that the most intense peaks in the spectrum are those of the $(CH_3CO)^+$ and $(M - CH_3CO)^+$ ions with m/e 43 and 257 respectively, due to the dissociation of the 17—20 double bond, i.e. a

process which is extremely unfavourable on energy grounds. To account for this anomaly, the authors suggested that this process involves a rearrangement accompanied by the migration of the CH_3 group from the 13-position to the 17-position and the formation of a stable allyl carbonium ion **aa**. On the basis of this single instance, the authors conclude that the dissociation of the double bond may be facilitated if it is associated with a simultaneous rearrangement. From our point of view, the formation of the $(M - CH_3CO)^+$ ion may be due to a preliminary migration in the molecular ion of the double bond to the 15—16 position followed by the dissociation of the 17—20 bond, which has become allylic, and the formation of the ion aa′:



M^+ (LXXIII, R = R′ = Me); (LXXIIIa, R = CD_3, R′ = Me); (LXXIIIб, R = Me, R′ = CD_3)

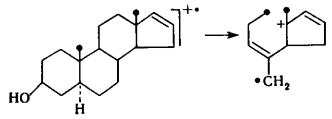
aa aa′

m/e 257 (R = Me); *m/e* 260 (R = CD_3); *m/e* 257 (R = Me).

Studies of the mass spectra of trideuteromethyl analogues of compounds (LXXIIIa and b) showed[72] that, in contrast to saturated pregnanes, in which the elimination of the CH_3 group from the 13-position does not occur, in the mass spectrum of compound (LXXIII) the peak of the $(M - 15)^+$ ion has been generated to the extent of 82% as a result of the loss of this particular methyl group.

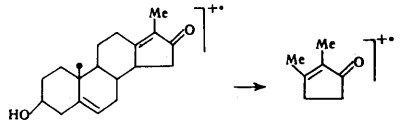
It is noteworthy that the elimination of the side chain from the $C_{(17)}$ atom is believed by many investigators[74-76] to be typical also for $\Delta^{13(17)}$-steroids, although they did not consider the mechanism of this process. Probably in the present case too there is a preliminary migration of the double bond to the 13—14 position with subsequent dissociation of the 17—20 bond, which has become allylic.

The peak of the ion with *m/e* 148, to which structure bb was ascribed, was detected in the mass spectrum of 5α-androst-16-en-3β-ol (LXXIV).[9] Von Unruh and Spiteller[55] believe that this ion is common to all steroids in which the structures of rings *B*, *C*, and *D* are analogous to those of compound (LXXIV):



M^+ (LXXIV) bb, *m/e* 148.

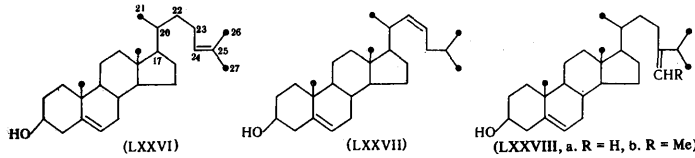
An interesting example of the effect of the double bond in ring *D* on decomposition under electron impact is provided by the mass spectrum of 3β-hydroxy-17-methyl-18-norandrosta-5,13(17)-dien-16-one (LXXV),[18] which shows a medium-intensity peak with *m/e* 110 (the ion bb) due to the dissociation of two allylic bonds 8—14 and 11—12 with migration of two hydrogen atoms to the charged fragment. Probably, as in the formation of the ion i (section II, 2), the driving force of this process in compound (LXXV) is provided by the αβ-unsaturated ketone grouping in ring *D*:



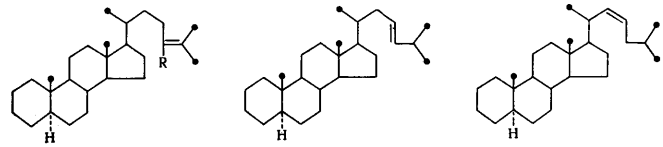
M^+ (LXXV) u, *m/e* 110.

VI. STEROIDS WITH A DOUBLE BOND IN THE SIDE CHAIN AT $C_{(17)}$

Wyllie and Djerassi[77] demonstrated for a large number of steroids with a double bond in different positions in the side chain at $C_{(17)}$ that the scission of the side chain is accompanied by the migration of two hydrogen atoms from the charged fragment. This distinguishes the above type of steroids from their saturated analogues which lose the side chain as a result of simple dissociation of the 17—20 bond. Thus the spectra of cholesta-5,24-dien-3β-ol (LXXVI), cholesta-5,22-dien-3β-ol (LXXVII), 24-methylenecholesterol (LXXVIIIa), and 24-ethylidenecholesterol (LXXVIIIb) show peaks with *m/e* 271, while in those of 5α-cholest-24-ene (LXXIXa), 5α-ergost-24-ene (LXXIXb), 5α-cholest-23-ene (LXXX), and 5α-cholest-22-ene (LXXXI) the mass numbers of the above peaks are displaced to *m/e* 257.

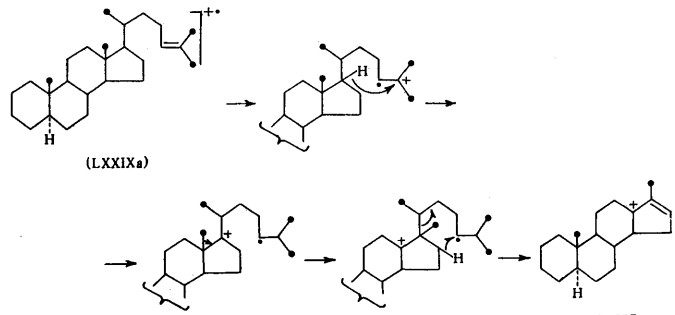


(LXXVI) (LXXVII) (LXXVIII, a. R = H, b. R = Me)



(LXXIX, a. R = H, b. R = Me) (LXXX) (LXXXI).

Analysis of the mass spectra of 17,22,22-D_3-, 15,15,17-D_3-, 12,12-D_2-, 14-D_1, and 16,16-D_2-analogues of (LXXIXa) showed that the rearrangement leading to the formation of the *m/e* 257 ion (dd) involves the hydrogen atom at $C_{(17)}$ to the extent of 100%, while the second hydrogen atom migrates from $C_{(12)}$ (35%), $C_{(14)}$ (10%), and $C_{(16)}$ (25%). The mechanism proposed[77] for the formation of the ion dd includes also the migration of the 18-CH_3 group to the $C_{(17)}$ atom, which leads to an allylically stabilised ion:



(LXXIXa)

dd, *m/e* 257.

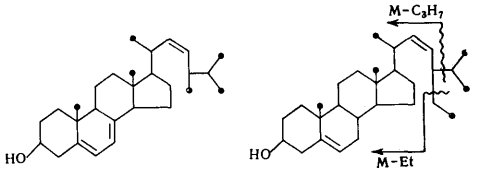
In Δ^{22}-steroids, the hydrogen atoms at $C_{(17)}$ (100%) and $C_{(14)}$ (55%) are involved in the formation of the ion dd, which has also been confirmed by the corresponding shifts in the mass spectra of the deutero-analogues[77].

The presence in the mass spectrum of the steroid of the peak due to the ion dd is evidence that it contains an unsaturated side chain at $C_{(17)}$ but does not provide information about the location of the double bond in it. As the position of the double bond is altered, the intensity of the peak due to the ion dd changes too, which has been recommended[77] as a feature suitable for diagnostic purposes. However, the mass spectra of steroids with

an unsaturated side chain contain many characteristic peaks, which reflect more rigorously the location of the double bond.

1. Δ^{22}-Steroids

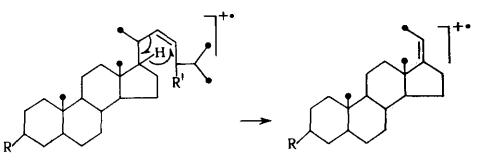
A characteristic feature of this group of steroids, together with the peaks of the ion dd, is the presence in the mass spectra of intense peaks caused by the elimination of the side chain at $C_{(17)}$ from the molecular ion without the migration of hydrogen atoms. The driving force of this process is provided by the dissociation of the 17—20 allylic bond. Thus the most intense peaks correspond to *m/e* 271 in the spectrum of ergosterol (LXXXII),[23,78] *m/e* 273 in the spectra of stigmasterol (LXXXIII)[47,77] and 7,8-dihydroergosterol (24-methylcholesta-5,22-diene-3β-ol),[77] and *m/e* 259 in the spectrum of 5α-cholest-22-ene (LXXXI).[77] In the mass spectra of the above compounds, all the peaks are present as doublets with those due to the ions dd differing from the peaks described above by 2 a.m.u.



(LXXXII) (LXXXIII).

In addition, the spectra of stigmast-22-en-3β-yl acetates (LXXXIV)[79] and (LXXXIII)[77] contain peaks due to the $(M - C_2H_5)^+$ and $(M - C_3H_7)^+$ ions produced as a result of the elimination of part of the side chain owing to the dissociation of other allylic bonds.

The mass-spectra of compounds (LXXXI)[77] and (LXXXIV)[79] also show peaks due to ions with *m/e* 344 and 286 (ee), caused respectively by the dissociation of the 20—22 double bond with transfer of a hydrogen atom from the charged species. It has been noted that for low ionisation energies the *m/e* 286 peak in the spectrum of compound (LXXXIV) becomes a maximum. Naturally when the molecule contains an acetoxy-group [for example, as in compound (LXXXIV)] the peak of the ion ee is accompanied by that of the $(ee - CH_3COOH)^+$ ion:



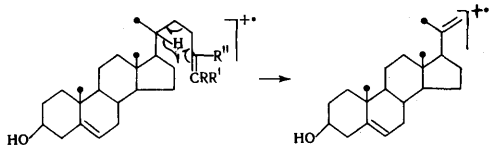
M^+ (LXXXI, R = R' = H); (LXXXIV, R = OCOMe, R' = Et) ee (R = H), *m/e* 286; (R = OCOMe), *m/e* 344

2. Δ^{23}-Steroids

The mass spectrum of 5α-cholest-23-ene (LXXX)[77] contains, together with the intense peak of the ion dd (*m/e* 257), an appreciable peak due to the ion with *m/e* 287 produced by the dissociation of the allylic 20—22 bond. When the ionising potential is reduced, the peak of the ion dd becomes dominant in the spectrum.

3. Δ^{24}- and 24-Alkylidene-derivatives of Steroids

In the mass spectra of compounds of this type, the peak of the ion dd is one of the most intense. On the other hand, the presence of very intense peaks of ions of type ff, generated by the dissociation of the allylic bond 22—23 with the elimination of a hydrogen atom, probably from the 20-position, is frequently characteristic of such compounds, for example (LXXVIIIa and b),[77] (LXXIXa and b),[77] desmosterol (LXXXV),[47] and many other 24-alkylidene-derivatives discussed by Knights and coworkers[47,80,81] and Benveniste et al.[82] Peaks of ions of type ff are characteristic only of the spectra of Δ^{24}- and 24-alkylidene-derivatives of steroids:

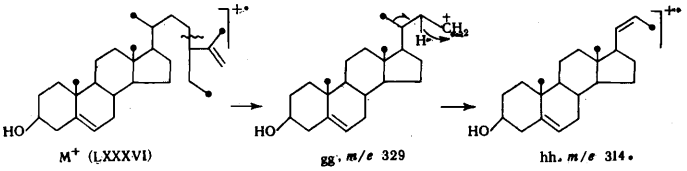


M^+ (LXXVIIIa, R = R' = H, R'' = C_3H_7); (LXXV, R = R' = Me, R'' = H) ff, *m/e* 314.

Galli and Maroni[52] noted that the most intense peaks in the spectra of cholesta-5,24-dien-3β-yl (XLVI) and cholesta-8,24-dien-3β-yl (LIX) acetates are those of the $(CH_3)_2C{=}\overset{+}{C}HCH_2$ ion with *m/e* 69, produced by the dissociation of the allylic 22—23 bond.

4. Δ^{25}-Steroids

The only example of a Δ^{25}-steroid, namely stigmasta-5,25-dien-3β-ol (LXXXVI), has been described by Wolfgang[83], who pointed out the presence in the spectrum of *m/e* 329 and 314 peaks, but did not discuss the question of their origin. We believe that the first (the ion gg) is due to the dissociation of the allylic 23—24 bond, while the second (the ion hh) may be formed as a result of the subsequent loss by the ion gg of one of the methyl groups, for example at $C_{(20)}$:[18]



M^+ (LXXXVI) gg, *m/e* 329 hh, *m/e* 314.

In conclusion of this section, we may note that in the majority of the studies quoted the decrease of the intensities of the characteristic peaks following the introduction of additional double bonds into the nucleus was considered. On the other hand, according to the observations of Knights[47], the appearance of a double bond in the side chain hinders certain processes characteristic of the decomposition of Δ^5- and Δ^7-steroids.

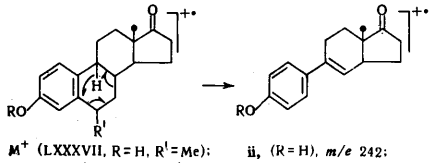
VII. AROMATIC AND DIENE STEROIDS

Certain aromatic and diene steroids were frequently mentioned in the previous sections but as a rule these were compounds with unsaturated centres fairly remote from one another which have little mutual influence and do not alter the fundamental decomposition pathways characteristic of each (see sections II, 2; III, 3; IV, 1; VI; VI, 1, 3, and 4). Aromatic and diene steroids containing conjugated or very close unsaturated centres, which

sometimes alters radically the fragmentation pattern characteristic of the corresponding monoenes, constitute a special group.

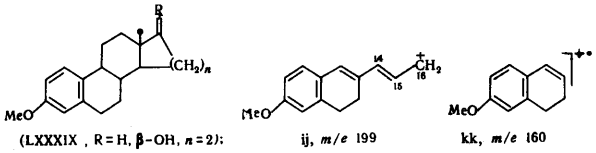
1. Aromatic Steroids

Djerassi et al.[69] investigated the mass spectra of many steroids with one and two aromatic rings, belonging to the group of oestrone and equilenin. The presence of the aromatic ring in these compounds greatly stabilises the molecular ion, the peak of which is as a rule dominant in the spectrum. In the high-molecular-weight region of the spectrum of 6-methyloestrone (LXXXVII) and the methyl ether of oestrone (LXXXVIII), there are intense peaks due to the $(M - C_2H_4)^+$ and $(M - C_3H_6)^+$ ions caused respectively by the elimination of the $C_{(6)}$ and $C_{(7)}$ atoms with formation of the ion ii:



M^+ (LXXXVII, R = H, R' = Me); (LXXXVIII, R = Me; R' = H) ii, (R = H), *m/e* 242; (R = Me), *m/e* 256

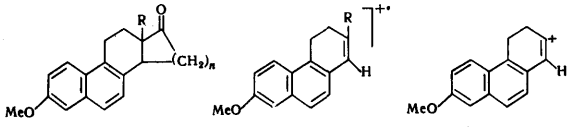
The peak of the *m/e* 199 ion (jj), for the formation of which a complex mechanism has been proposed involving the loss of the $C_{(11)}$–$C_{(13)}$ and $C_{(17)}$ atoms, is one of the most characteristic in the spectra of compound (LXXXVIII) and its stereoisomers. The peak is observed also in the spectra of the stereoisomers of the methyl ether of oestradiol (LXXXIX) [27,70] and the methyl ether of D-homo-oestrone (XC).[84]



(LXXXIX, R = H, β-OH, *n* = 2); (XC, R = O, *n* = 3) ij, *m/e* 199 kk, *m/e* 160

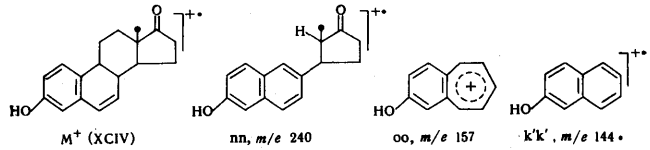
The mass spectra of all the compounds considered above, and also of their 14-hydroxy-derivatives (LXVI, a–c) [71] contain intense peaks due to *m/e* 160 ions (kk) formed as a result of the dissociation of the 8–14 and 9–11 bonds and the ion w with *m/e* 186 (see section IV, 1).

In the mass spectra of the methyl ether of equilenin (XCI),[69] its 18-nor-13-ethyl-analogue (XCII),[69] and the methyl ether of D-homoequilenin (XCIII),[84] there are also intense peaks due to molecular ions. On the other hand, the characteristic peaks are those of the "tricyclic ions" ll and mm, the formation of which involves the dissociation of bonds in ring *D*:



(XCI, R = Me, *n* = 2); (XCII, R = Et, *n* = 2); (XCIII, R = Me, *n* = 3) ll, (R = Me), *m/e* 224; (R = Et), *m/e* 238 mm, *m/e* 209

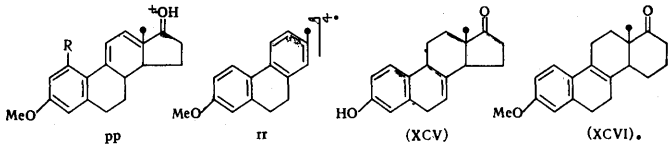
In the spectrum of Δ^6-dehydro-oestrone (XCIV) [69] there is an intense M – 28 peak (the ion mm), the formation of which probably involves the elimination of an ethylene molecule from ring *C*. The most intense peaks in the spectrum of compound (XCIV) with *m/e* 157 and 144 most probably correspond to the ions oo and k'k' respectively:



M^+ (XCIV) nn, *m/e* 240 oo, *m/e* 157 k'k', *m/e* 144.

The mass spectrum of equilin (XCV) [69] differs from that of compound (XCIV) only by a lower intensity of the peak due to the ion oo.

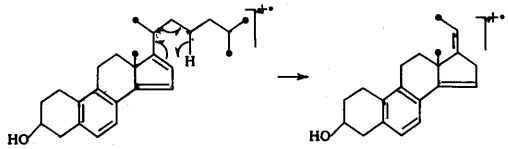
The peaks due to $(M - 15)^+$ ions, which may have the structure pp, are dominant in the mass spectra of the methyl ether of $\Delta^{9(11)}$-dehydro-oestrone and its 1-methyl analogue (LXIVc) (see section IV, 1).[69] Another characteristic feature of the spectra of these compounds is the presence of an M – 57 and M – 58 double peak (the ion rr) due to the loss of ring *D*:



pp rr (XCV) (XCVI).

The characteristic ions derived from the methyl ether of Δ^8-dehydro-D-homo-oestrone (XCVI),[27] as for the methyl ether of equilenin (XCI), are those formed as a result of the dissociation of bonds in ring *D*, namely the 6,7-di-hydro-analogues of the ions ll and mm.

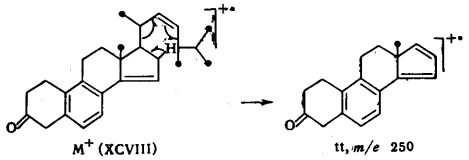
The peak of the ion corresponding to the loss of part of the side chain at $C_{(17)}$ with migration of a hydrogen atom to the charged species ss has been detected by Brown and Turner[85] in the mass spectrum of cholesta-5(10),6,8,14,16-pentaen-3β-ol (XCVII). Presumably the driving force in this process comes from the dissociation of the allylic 20–22 bond accompanied by the migration of the double bond and the transfer of a hydrogen atom via a six-membered transition state:



M^+ (XCVII) ss, *m/e* 280.

However, on the basis of this one example, it is impossible to say whether the process is determined by the Δ^{16}-bond alone or whether it can occur only in the presence of a conjugated system of double bonds.

In ergosta-5(10),6,8,14,22-pentaen-3-one (XCVIII),[85] the side chain is eliminated as a result of the rupture of the allylic 17–20 bond accompanied by the elimination of a hydrogen atom from the charged species (the ion tt).



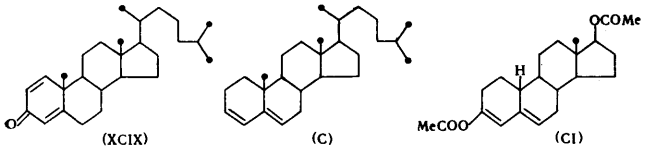
M^+ (XCVIII) tt, *m/e* 250

Apparently the elongation of the conjugation chain provides the driving force for the formation of the ion tt.

2. Diene Steroids

The intense peak of the ion with m/e 122 is the most characteristic of the mass spectrum of cholesta-1,4-dien-3-one (XCIX).[22] It is probably formed via a mechanism similar to that of the formation of the ion 1 (see section II, 2) from which it differs by two mass units, as expected.

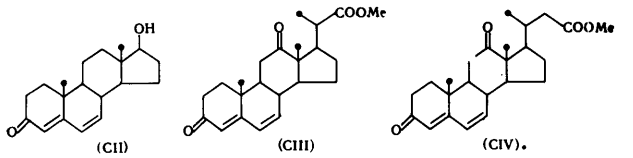
Galli and Maroni[52] believe that the most characteristic type of fragmentation of cholesta-3,5-diene (C) involves the formation of the ion p' with m/e 120 (see section III, 1) as a result of type RDR decomposition in ring B. The peak of an analogous ion with m/e 122 is observed also in the spectrum of 19-norandrosta-3,5-diene-3,17β-diyl diacetate (CI).[18] When the molecular ion of compound (CI) decomposes, a molecule of keten is initally eliminated from the 3-CH_3COO group (a process characteristic of enol acetates) and the resulting radical-ion undergoes a further type RDR decomposition). Moreover, ions with m/e 147 (tt) and 161 (uu) are formed from the $(M-CH_2=C=O)^+$ ion.



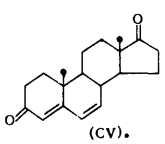


The mass spectrum of cholesta-2,4-diene (XI) (see section II, 2) is not very characteristic[18] but in the region of low mass numbers it contains a very specific triplet of peaks with m/e 105–107. The formation of ions responsible for these peaks probably involves the dissociation of the 6–7 and 9–10 bonds and the location of the charge on ring A.

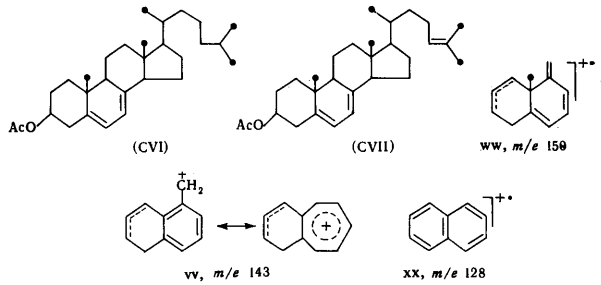
In the mass spectrum of 17β-hydroxyandrosta-4,6-dien-3-one (CII),[9,23] there are intense peaks due to ions with m/e 136 and 157, the origin of which has not, however, been elucidated. These peaks are also observed in the mass spectra of the methyl esters of 3,12-dioxobisnorchola-4,6-dienoic (CIII)[38,39] and 3,12-dioxonorchola-4,6-dienoic (CIV)[38] acids:



Recently Orr and Broughton[86] also observed the peak of the m/e 136 ion in the mass spectrum of androsta-4,6-diene-3,17-dione (CV) and explained its origin by the dissociation of the 9–10 and 7–8 bonds and the migration of two hydrogen atoms to the charged fragment containing ring A and part of ring B. When the charge is located in the other part of the molecule with migration of a hydrogen atom away from it, an ion with m/e 149 is formed with the dissociation of the same bonds, its peaks being approximately three times less intense than that of the first ion:



Galli and Maroni[52] have analysed the mass spectra of cholesta-5,7-di-en-3β-yl (CVI) and cholesta-5,7,24-trien-3β-yl (CVII) acetates. The authors noted intense peaks due to ions with m/e 143 (vv) and 158 (ww) and a small peak with m/e 128 (xx).



---o0o---

Thus the entire data analysed above demonstrate that the mass spectra of steroids with double bonds in the 1–2, 2–3, 4–5, 5–6, 7–8, 13–14, 16–17, 22–23, 23–24, and 24–25 positions are very characteristic which as a rule makes it possible to infer unambiguously the location of the double bond in the steroid nucleus or in the side chain by analysing the mass spectra. The double bonds in other positions either do not initiate specific decomposition pathways of the molecular ions or give rise to processes which are difficult to interpret from the standpoint of the current hypothesis of the preferential dissociation of the weakest bonds. In certain cases the insufficient number of examples investigated precludes a generalisation. Steroids with several double bonds remote from one another decompose via pathways initiated by each separately. The inclusion of double bonds in the conjugated system gives rise to special decomposition pathways which are not characteristic of compounds with the corresponding isolated double bonds, and the stability of the molecular ion increases appreciably.

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Shemyakin Institute of the
Chemistry of Natural
Products, USSR Academy
of Sciences

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N-Acylpyridinium Salts and Corresponding Fused Benzo-derivatives

A.K.Sheinkman, S.I.Suminov, and A.N.Kost

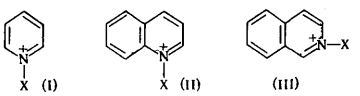
Published information on the preparation, structure, and reactions of *N*-acylpyridinium salts and the corresponding benzo-derivatives is summarised. They comprise purely ionic structures with the acyl group attached to the nitrogen atom, which bears a positive charge (partly delocalised through the ring), and a halide counter-ion. In individual cases (quinolinium and isoquinolinium) the electron of the anion may be transferred to a non-bonding orbital of the heterocycle with formation of a charge-transfer complex. *N*-Acylated heterocyclic cations contain more than one reaction centre, and are capable of *trans*-acylation, ring opening, hetarylation, one-electron reduction, etc. Processes involving hetarylation are especially interesting, and permit the preparation of various difficultly accessible derivatives of pyridine, quinoline, isoquinoline, and acridine. A list of 419 references is included.

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I. INTRODUCTION

A systematic survey is made of published data on the preparation, structure, and chemical reactions of *N*-acyl derivatives of six-membered nitrogen heterocycles—pyridine and its benzologues

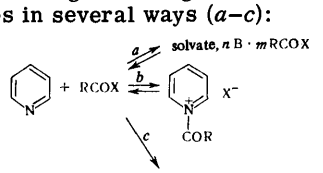


as well as their analogues—where X represents an electron-accepting group—RCO, $CONR_2$, COOR, sometimes CN, phosphoryl groups PO_3^-, PO_3R, $NH_3PO_2^-$, etc.

Although several reviews and monographs have been devoted to quaternary pyridinium, quinolinium, and isoquinolinium salts[1-4], the general aspects of *N*-acylated heterocyclic cations have not been considered: there are only brief summaries of already obsolete literature on *N*-acylpyridinium salts in papers on other topics[2,5,6]. During the past 10–15 years development of the acylation and phosphorylation of various nucleophilic compounds by salts of *N*-acylated heterocyclic cations (sometimes formed *in situ*) has been accompanied by elaboration of a method for introducing a heterocyclic ring into compounds containing an acidic methine group (ketones, dialkylanilines, pyrrole, furan, etc.), and several new reactions have been discovered. All this demands our attention.

II. PREPARATION AND STRUCTURE OF *N*-ACYL-PYRIDINIUM SALTS AND CORRESPONDING FUSED BENZO-DERIVATIVES

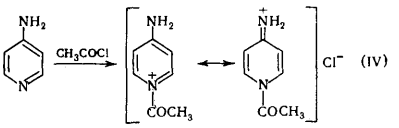
Pyridine and analogous nitrogen bases are able to react with acid halides in several ways (*a–c*):



When pyridine is carefully mixed with acetyl chloride in ether or petroleum ether, heat is evolved, and after cooling solid acetylpyridinium chloride is precipitated[7-9]. Other workers[10-12], however, were able to isolate only pyridine hydrochloride and keten, with part of the latter polymerising to dehydracetic acid[11,13,14]. Quinoline, 2-methylquinoline, and 2,6-dimethylpyridine under these conditions form mixtures of their hydrochlorides and the corresponding adducts with acetyl chloride[10,15]. If the reaction is conducted in chloroform, which dissolves pyridine hydrochloride, especially at low temperatures, *N*-acetylpyridinium chloride of greater purity can be obtained[12].

N-Acylpyridinium chlorides are prepared by adding pyridine to an equivalent quantity of the acyl chloride in anhydrous ether, benzene, petroleum ether, or dry nitrogen in the absence of a solvent[16-26]. Only pyridine hydrochloride is formed when the reactants are added in the opposite sequence. The method can be used to prepare quinoline and 2-methylquinoline salts[27,28]. Methylpyridines react with acetyl chloride in the cold to form compounds of variable composition, which are unstable on keeping[9,29].

The stability of *N*-acetylpyridinium salts is increased by the presence of substituents capable of helping to delocalise the positive charge[25,30,31]. Treatment of 4-aminopyridine in ether with acetyl chloride (as well as with benzoyl and toluenesulphonyl chlorides) produces salts of the type (IV):



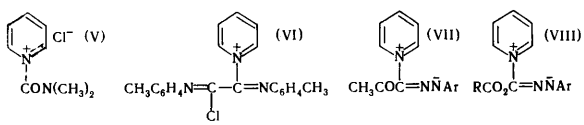
1-Acetyl-4-dimethylaminopyridinium chloride is evidently still more stable[25,30], but a very unstable quaternary salt is obtained by the action of acetyl chloride an 4-acetamidopyridine in oxolan[30].

Benzoyl chloride and quinoline form the adduct $C_9H_7N.2C_6H_5COCl$,[32] but equivalent quantities of the reactants generally yield a mixture of an *N*-benzoylquinolinium chloride and the hydrochloride of the base[33]†. It has not

†Reissert[34,35] was unable to isolate a product from the reaction of benzoyl chloride with quinoline, but obtained the corresponding "pseudobase" on attempting the Schotten–Baumann synthesis (with aqueous alkali).

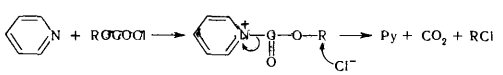
hitherto proved possible to isolate pure *N*-benzoylpyridinium chloride [8,12,17,32], but aroyl chlorides containing electron-accepting substituents in the ring form stable *N*-acylpyridinium salts [7,16]. Olah [36] has recently reported the preparation of *N*-acetyl-, *N*-propionyl-, and *N*-benzoylpyridinium hexafluoroantimonates by acylating pyridine with solutions of carboxonium salts in sulphur dioxide. *N*-Nitro- and *N*-nitroso-pyridinium fluoroborates have been prepared similarly [37]. Information on salts of pyridinium bases, benzoyl chloride, and Lewis acids will be found in Ref. 31.

The adducts formed by pyridine, quinoline, and isoquinoline with carbamoyl chlorides, e.g. (V), are very stable [38-43]. Similar salts have been obtained also with 4-methylpyridine, 3,5-dimethylpyridine, and nicotinamide [42,44,45].



Pyridine and its homologous react with imidoyl chlorides of the type (o-$CH_3C_6H_4N$: $CCl)_2$, CH_3COCCl: : NNHAr, [46,47] and ArNHN : CClCOOR [48] to form stable compounds (VI)–(VIII).

According to the patent literature [49-56] adding carbonyl chloride, perchlorocarbonates, or alkyl chlorocarbonates to pyridine or 2-methylpyridine in benzene results in the rapid formation of precipitates containing 2 moles of base per mole of acylating agent, which react smoothly with water and aliphatic alcohols to produce symmetrical or unsymmetrical carbonates [57]. Repeated observations have since been made of the formation of adducts of pyridine, 2-methylpyridine, and quinoline with ethyl chlorocarbonate [58-63], but the products could not be isolated in a pure form. The adducts decompose when the temperature is raised. Carré has studied the breakdown of various chlorocarbonates in pyridine and quinoline [60,64,65], and demonstrated the high catalytic activity of the first of them:

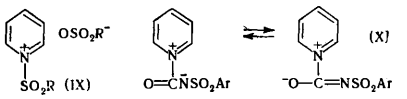


Information is available [66,67] on the reaction of carbonyl chloride with quinoline and 4,4′-bipyridyl.

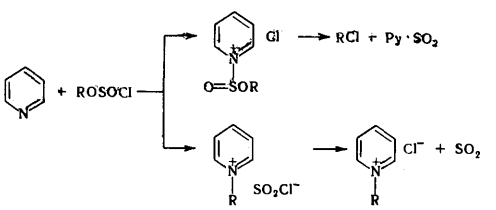
Similarly to the above example with acetyl chloride, treating 4-dimethylaminopyridine with t-butoxycarbonyl chloride in dry ether at 0°C yields the corresponding *N*-acyl salt [68].

Pyridine, quinoline, isoquinoline, and 4-methylpyridine readily form adducts with various substituted arenesulphonyl chlorides $RC_6H_4SO_2Cl$. [69-72] The stability of such salts diminishes in the sequence—isoquinoline, pyridine, quinoline [70]—and 2-methylpyridine probably does not react at all [69,74]. With polysulphonyl chlorides the reaction may cease on the replacement of one chlorosulphonyl group [71]. It has also been reported that *p*-acetamidobenzenesulphonyl chloride does not react with triethylamine and pyridine in anhydrous acetone [74,75]. The enhanced stability of *N*-arenesulphonylpyridinium salts in comparison with the *N*-acyl salts is shown in the possibility of obtaining adducts (IX) from anhydrides of methane- and benzene-sulphonic acids [73,76].

It is interesting that the condensation of isocyanatosulphonyl chloride $OCNSO_2Cl$ with pyridine involves only the sulphonyl group [78]. Yet the reaction of nitrogen bases with arenesulphonyl isocyanates usually leads to betaines of the type (X): [77,79]

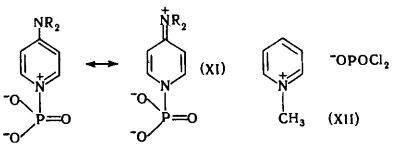


The reactions of pyridine and other tertiary amines with chlorosulphates $ROSO_2Cl$ have been surveyed in detail [80]. The normal products are alkyl halides and the complex $C_5H_5N.SO_3$, formed by breakdown of intermediate quaternary salts $ROSO_2\overset{+}{N}C_5H_5 + Cl^-$. [80,81] Pyridine reacts with alkyl chlorosulphinates to form mixtures of *N*-acyl and *N*-alkyl salts [82,83]:



The reactions of pyridine and its derivatives with thionyl chloride, sulphuryl chloride, chlorosulphuric acid, phosphoryl chloride, and other inorganic chlorides have also been studied [35,84,85].

Several quaternary pyridinium salts have been prepared containing a phosphoric-acid residue attached to the nitrogen atom. Treatment of 4-dimethylamino- and 4-morpholino-pyridines in benzene solution with excess of phosphoryl chloride and triethylamine followed by alkaline hydrolysis gave the salts (XI) as amorphous white powders [25,86]:



Analogous salts of 4-amino-, 4-isopropylamino-, and 4-dimethylamino-pyridines have been obtained by exchange with an *N*-phosphoryl salt of *N*-methylimidazole [25,87].

The possible formation of *N*-acyl derivatives also in the preparation of organophosphorus compounds by the reactions of acid chlorides and chloro-esters of phosphorus in the presence of pyridine and quinoline has been discussed [83,88], but few adducts have been isolated [84,89,90], and information on their structure is frequently lacking. The reaction may involve the O–R bond, not the phosphorus atom: thus the salt (XII) alone is formed from methyl phosphorodichloridate and pyridine [91].

A saltlike structure for the 1 : 1 adducts of pyridine with acyl chlorides was already suggested in the earliest papers [12,92]. Such a structure is indicated by the insolubility of the adducts in most non-polar solvents, the possibility of recrystallising the most stable compounds, the relatively high melting points, the reactions involving exchange of the anion, and the rapid and unambiguous acylations involving such adducts. Alternatively it was postulated that these adducts were complexes or even molecular compounds. It can now be accepted that the adducts are ionic structures with the acyl group attached to the nitrogen atom of the pyridinium ring and the halogen acting as counter-ion. This is based on the results of electrical conductivity measurements, polarography, heats of mixing, acid–base titrations, kinetic methods,

and ultraviolet, infrared, and nuclear magnetic resonance spectroscopy.

Paul and his coworkers [9,15,29,32,38,93] made visual and conductometric titrations of pyridine, methylpyridines, quinoline, and dimethylaniline in acetyl and benzoyl chlorides with titanium tetrachloride, tin tetrachloride, or arsenic pentachloride. The nitrogen heterocycles reacted with the Lewis acids (acceptors of the chloride ion) completely, giving one or two neutralisation points corresponding to the formation of "normal" and "acid" salts [15,29,93,94]. The same workers found appreciable electrical conductivity in solutions of the three methylpyridines and quinoline in acetyl chloride, although rather less than with benzyltrimethylammonium chloride. A mixture of pyridine and acetyl chloride in liquid sulphur dioxide at −30°C exhibited a complicated conductance corresponding in magnitude to the purely ionic salts $(C_2H_5)_3NH^+SbCl_6^-$ and $R_3O^+SbCl_6^-$. The strongly ionising solvent plays a definite part in this, of course.

Holeček [96] studied the electrical conductivity of solutions of pyridine, isoquinoline, quinoline, and acridine in acetyl bromide, and showed that they form adducts $[B.CH_3CO]^+Br^-$, which behaved as univalent electrolytes. The ionisation constants were 0.7×10^{-4} for the pyridine salt and $1.8–1.9 \times 10^{-4}$ for the quinoline, isoquinoline, and acridine salts. Korshak et al. [97] have recently determined potentiometrically the thermodynamic equilibrium constants for the reaction of benzoyl chloride with pyridine and triethylamine in acetonitrile. The higher value for pyridine than for triethylamine (1.2×10^{-4} and 2×10^{-5}), in spite of the less basic character of the former, was attributed to resonance factors enhancing the stability of the *N*-benzoylpyridinium salt.

The possibility of mesomerism is slight with unsubstituted *N*-acylpyridinium salts [95,98], and this is responsible for their relative instability.

1-Dimethylcarbamoylpyridinium chloride (V) behaves in aqueous solution as a strong electrolyte. This applies also to acetonitrile solutions, but the picture is then complicated by partial breakdown of the salt into its components as a result of solvolysis [42]. The conductance of solutions of *N*-diphenylcarbamoylisoquinolinium chloride in nitrobenzene has been studied recently [43]. A solution of benzoyl chloride and pyridine in 89% aqueous acetone conducts electricity and is able to benzoylate butylamine [99]. Although arenesulphonyl chlorides do not conduct electricity in nitromethane or liquid sulphur dioxide, considerable conductance is observed in the presence of pyridine and quinoline.

Paul [100,101] determined calorimetrically the heats of dissolution of 2-methylpyridine, quinoline, and dimethylaniline in acetyl and benzoyl chlorides, and also their heats of neutralisation by Lewis acids. The dependence of the enthalpy change on the concentration of the base showed in all cases a characteristic break at low concentrations, indicating increased dissociation of the solvates under these conditions.

On polarography in pyridine, acylpyridinium salts exhibit a typical reduction curve with two waves (half-wave potentials 0.1–0.7 and 1.3–1.7 V). [16,17,102] Similar results were obtained with mixtures of benzoyl or *p*-methoxybenzoyl chloride with pyridine, which suggests in these cases also the formation of acylpyridinium salts *in situ* [16,17].

Detailed studies have been made of the infrared spectra of *N*-acetyl- and *N*-propionyl-pyridinium chlorides [16–18], acetyl-pyridinium, -quinolinium, -isoquinolinium, and -acridinium bromides [103], and adducts of acetyl and benzoyl chlorides with pyridine and 3- and 3-methylpyridines [104]. Several papers mention the positions of individual bands in the infrared spectra of other salts [30,31,42,66,105,106].

Most workers note a shift in the carbonyl-stretching band (1760–1800 cm^{-1}) to higher frequencies (1790 to 1804 cm^{-1}) with *N*-acylpyridinium chlorides derived from aliphatic and aromatic acids. Such displacement indicates the presence of a positively charged cyclic nitrogen atom beside the carbonyl group. Although a larger shift is to be expected from the difference in values of the Taft constants for NR_3^+ and Cl, the replacement of Cl in the acyl chloride by NR_3^+ has the opposite effect by increasing the C—C—N angle [18]. This has been found also with aliphatic acylammonium salts [95,107–109].

Data on the ultraviolet spectra of solid *N*-acylpyridinium salts are restricted to examples of 1-acetyl-4-dialkylaminopyridinium chlorides [30,31], 1-dimethylcarbamoylpyridinium chloride [42,68], and 4-alkylamino-1-phosphorylpyridinium salts [25,86]. Conversion of a nitrogen base into an *N*-acyl salt is accompanied by a considerable bathochromic shift, while the absorption characteristic of the aromatic ring is maintained. Kinetic studies of the hydrolysis of acetic anhydride and reactions involving the transfer of acyl [20,110] have recorded the ultraviolet spectra of *N*-acyl derivatives of alkylpyridines obtained *in situ*, the differential spectra corrected for absorption by pyridine and its salt giving for acetylpyridinium λ_{max} = 272 and 255 nm (ϵ = 4300 and 7000).

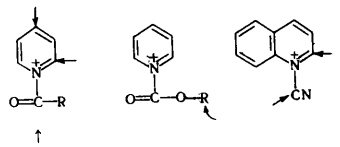
Data on the proton magnetic resonance spectra of these compounds are also fragmentary [25,30,36,37,42,68,86]. The chemical shifts of the 2-, 3-, and 4-protons of 1-acetyl-, 1-propionyl-, and 1-benzoyl-pyridinium fluoroantimonates in liquid sulphur dioxide (at −60°C) increase with increase in the accepting properties of the acyl group in this sequence [36] (cf. spectra of quaternary pyridinium salts [111]), which correlates with hetarylation experiments on these salts [112]. The chemical shifts also agree well with the expected values for pyridinium, *N*-nitrosopyridinium, and *N*-nitropyridinium fluoroborates [37].

On passing from 1-acetyl-4-dimethylaminopyridinium chloride to its analogue containing the less strongly electron-accepting 1-t-butoxycarbonyl group we observe the same decrease in chemical shift for both 2- and 3-protons [30,68], although the infrared spectra indicate that the charge on the former is more strongly delocalised (νCO = 1755 and 1770 cm^{-1}). It is more difficult to analyse the nuclear magnetic resonance spectra of 4-amino-1-phosphorylpyridinium [25,86]. The contribution of immonium forms to resonance stabilisation would probably be greater for the dimethylamino- than for the isopropylamino-group (cf. XI). This diminishes appreciably the deshielding of the 2-protons in the former case, which is shown in the chemical shifts (8.2 and 8.6 ppm). The opposite relation is found for the 3-protons.

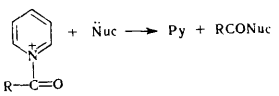
In view of the possible involvement of *N*-acylpyridinium salts in acylation by acid anhydrides, many attempts have been made to detect by infrared and n.m.r. spectroscopy their presence in solutions of pyridine and an anhydride [19,112–116]. In non-polar solvents such as carbon tetrachloride no significant changes are observed in the spectra when pyridine is mixed with acetic and trifluoroacetylacetic anhydrides [113,114,116]. Similarly, the ultraviolet spectra of pyridine–acetic anhydride mixtures in cyclohexane are additive [113]. In the acetic anhydride–1,4-diazabicyclo[2,2,2]octane system, however, formation of the corresponding *N*-acyl salt can be established from the infrared and n.m.r. spectra or refractometrically [114].

III. REACTIVITY OF *N*-ACYLPYRIDINIUM SALTS AND CORRESPONDING FUSED BENZO-DERIVATIVES

N-Acylpyridinium salts and the corresponding fused benzo-analogues contain more than one reaction centre both in the ring system and in the acyl group. In conformity with this their reactions can be divided into six main types.

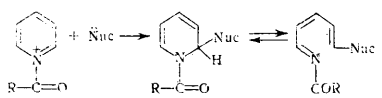


1. Attack by nucleophilic reagents on the exocyclic carbon atom attached to the heteroatom leads to elimination of the nitrogen base and transfer of the acylating group to a component of the medium (acylation of water, alcohols, amines, acids, etc.) or to the gegenion (solvolysis)[42,102]:



We must include here reactions in which the acyl group is transformed—hydrolysis of nitrile to amide[106], decomposition of acyl salts of chlorocarbonates, chlorosulphates, etc. effected by attack by the gegenion (Cl^-) on the C–O–R bond[55,65,80], formation of ketens (attack by the pyridine ring on an α-proton relative to the carbonyl group)[117,118].

2. Attack by a nucleophilic reagent at the 2-carbon atom of the heterocycle, yielding so called "pseudobases" or more often opening the ring (Zincke–König reaction)[3,119]:



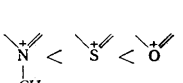
3. Addition of nucleophilic reagents at the 2- and 4-positions of the heterocyclic ring results in the formation of 1-acyl-1,2(or 4)-dihydro-derivatives or, if these are unstable, to substituted heterocycles (after detachment of the acyl groups and aromatisation). These reactions, which can be combined under the name "hetarylation", are of the greatest interest, since they permit the preparation of various compounds, including naturally occurring substances, that are often inaccessible by other methods.

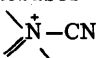
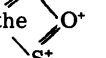
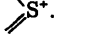
4. Reactions involving one-electron transfer to the *N*-acyl salts followed by dimerisation of the radicals (Dimroth reduction)—or radical hetarylation.

5. Reactions involving methyl or methylene side-groups activated by the presence of the *N*-acyl group[17,28,120,121].

6. Electrophilic substitution in salts of *N*-acylated heterocyclic cations[122,123].

Reactions of types 3–5 are known for various aromatic and heterocyclic cations—tropylium, cyclopropenylium, pyrylium, thiapyrylium, etc.—which is evidence of the similarity of their π-electron systems. The effect of substituents is transmitted through the positively charged nitrogen atom[111,124], although probably not by conjugation but purely by induction. In this connection the sequence of increasingly strong electron-accepting properties of the heteroatoms



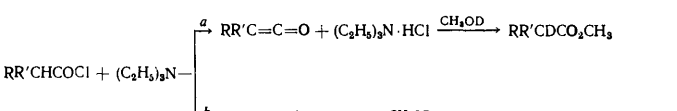
found for pyrylium, thiapyrylium, and pyridinium salts[125] should change significantly if a strongly electron-accepting substituent is attached to the cyclic nitrogen atom. By comparing values of pK_{ROH} for a series of pseudobases Johnson has shown[126] that the acceptor effect of the  group in *N*-cyanoquinolinium approaches that of the  group in benzopyrylium and exceeds the effect of  .

1. Acylation in the presence of Pyridine Bases

Examples of the use of pyridine in the acylation of alcohols and phenols date from the 1890s (bibliography in Ref. 127), but pyridine was regarded initially merely as a substitute for alkali. The advantages and limitations of this method were studied on many hydroxy-compounds and acylating agents by Einhorn and Hollandt[127], and hence the term "Einhorn acylation" is encountered in the literature[128,129a–131a].

Acylation in pyridine is effective for alkali-sensitive compounds. Pyridine is a good solvent, and therefore acid chlorides can be replaced by acids with subsequent addition of chlorinating agents (e.g. carbonyl, thionyl, and benzoyl chlorides) or the experimentally more convenient acid anhydrides (especially acetic anhydride). Acylation in the presence of pyridine takes place also in acid media. Even under these conditions the acylpyridinium chloride is evidently formed[127]. The use of acetic formic anhydride or a mixture of formic acid with acetic anhydride and pyridine has recently been recommended for the formylation of aliphatic and cycloaliphatic alcohols[132]. Pyridine compounds also play an important part in the preparation of chlorocarbonic esters, carbonates, chlorosulphates, and several other compounds having mixed functions[51,55,80,133]. If the hydroxy-compounds are replaced by their alkoxides, only traces of pyridine are required, since it is regenerated in the course of the exchange reaction.

The high acylating power of individual *N*-acylpyridinium salts towards alcohols and phenols is confirmed by direct experiments[23,51,53,57]. Addition products of carbonyl chloride and pyridine bases[53,54,86] effectively phosgenate alcohols, phenols, naphthols, anilines, and cyclic imines. Although *N*-nitropyridinium fluoroborate is unsuitable for the nitration of aromatic compounds, it does *o*-nitrate water and alcohols[37]. There is indirect confirmation of the involvement of acylammonium salts in acylations[134,135]. Aliphatic acid chlorides react with CH_3OD in triethylamine to form a mixture of $RR'CDCOOCH_3$ and $RR'CHCOOCH_3$, produced by two competitive reactions[136]:



Path (*a*) predominates or is the sole reaction with acid chlorides that are sterically hindered at the reaction centre, since they have less effect at the stage of elimination of the α-hydrogen atom (acid–base equilibrium) than on formation of the quaternary acyl salt. The percentage inclusion of deuterium in acetyl halides falls in the sequence Cl > Br > I > CH_3COO, i.e. with improvement in the so called "leaving group"[137–139].

Such data are lacking for esterification in pyridine, but the weakness of pyridine bases compared with triethylamine, together with the greater resonance stabilisation

of *N*-benzoylpyridinium than of benzoyltriethylammonium [95,97,98], leads us to expect reaction (*b*) alone, at least with sterically unhindered acid chlorides. Individual monographs, however, have hitherto assigned to pyridine bases the role merely of participation in acid–base equilibria (proton acceptor) [140].

The preparation of arenesulphonates of alcohols and phenols is also often conducted in pyridine [6,129b,130a,131b,141,142], again with intermediate formation of arenesulphonylammonium salts [70,71,73,75,76]. In most cases higher yields are obtained than with aqueous sodium hydroxide. Sometimes, however, the resulting esters (especially of lower alcohols) alkylate the pyridine to form alkylpyridinium salts, which lowers the yield. It has therefore been recommended that pyridine should be replaced by 2,6-dimethylpyridine, although this slows down the process significantly [143]. In the arenesulphonylation of 1,4- and 1,5-diols, certain amino-alcohols, and γ-hydroxy-amides the intermediate monosulphonate may be cyclised with the formation of various oxygen and nitrogen heterocycles (see Refs. 131b, 144, and 145 and the bibliography given there). Kröhnke has prepared aldehydes via quaternary pyridinium salts [6,141].

Systems comprising a carboxylic acid and pyridine with benzenesulphonyl or toluene-*p*-sulphonyl chloride have an acylating, not an arenesulphonylating, action [145]. They yield esters with primary and secondary alcohols, phenols, and polyphenols. This method is mostly used for the acylation of tertiary alcohols liable to dehydration. The reaction is assumed to involve the formation of acid anhydrides *in situ*, with regeneration of the arenesulphonyl chloride:

$$(RCO)_2O \xrightarrow[\text{TosCl + Py}]{R'OH} RCO_2H + RCO_2R'$$

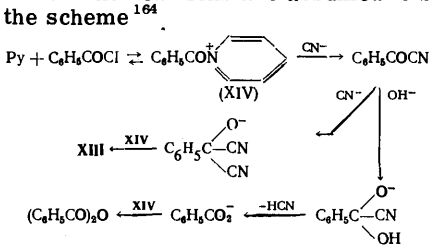
For the analytical application of acylations see Refs. 114, 128, 140, and 146–150.

Similarly, *N*-acylpyridinium salts react with carboxylic acids to form anhydrides or mixed anhydrides:

$$\left[RCO\text{-}\langle\text{pyridinium}\rangle\right] Cl^- + R'CO_2H \rightarrow RCOOCOR' + Py \cdot HCl$$

This reaction, discovered as early as 1892, [92,151–153] has not lost its importance for the preparation of anhydrides even at the present time. To obtain symmetrical anhydrides it is sufficient to act with water on a mixture of the acid chloride and pyridine (better in an inert organic solvent). No advantage is generally obtained by using a mixture of the acid chloride and the carboxylic acid or alkaline additives (sodium carbonate, barium carbonate, sodium hydrogen carbonate) to combine with the hydrogen chloride. At various times this method has been used to obtain anhydrides of substituted benzoic acids [8,92,151,154–157], cinnamic acid [151], several aliphatic acids [8,40,151,154,156] including α-chloro-acids, and certain heterocyclic acids [8]. Acid chlorides can also be employed *in situ*, by introducing into a solution of pyridine and the acid either carbonyl chloride or thionyl chloride [53,158,159] or a mixture of an arenesulphonyl chloride and an acid [145]. The possibility that solid adducts of acyl chlorides and pyridine are involved in these condensations has been demonstrated many times [8,22,23,40,53,160]. Mixed anhydrides are usually prepared by adding acetyl and benzoyl chlorides or chloroformic esters to a mixture of a relatively unreactive acid and pyridine in ether or benzene, and then treating with ice [153,161,162].

Still greater simplifications have recently been introduced into the preparation of anhydrides [163]. If the acid halide and the reaction product are comparatively stable towards water, the chloride can simply be added to an aqueous solution of an equivalent quantity of the sodium salt of the acid in the presence of catalytic quantities of pyridine, 3-aminopyridine, or pyridine *N*-oxide. Some decrease in yield occurs with methylpyridines, while the reaction is not catalysed by 2- and 4-aminopyridines, 2-fluoropyridine, or any pyridinecarboxylic acid. Aqueous *N*-benzoylpyridinium chloride acylates also salts of certain inorganic acids: e.g. benzoyl azide is obtained in 85% yield with sodium azide. An analogous reaction was described [8] with hydrogen sulphide in petroleum ether at −20°C. When benzoyl chloride is shaken with aqueous potassium cyanide and pyridine (1 : 1 : 1), however, the resulting benzoic anhydride is accompanied by the so called "dimer of benzoyl cyanide" $R.C_6H_4CO.O.C(CN)_2.C_6H_4.R$ (XIII); with chlorides of substituted benzoic acids dimeric products are formed as byproducts or as the main products [163,164]. The reactions are assumed to be represented by the scheme [164].



The controlled hydrolysis of acid chlorides in the presence of pyridine has been employed also in the preparation of tetra-alkyl pyrophosphates and mixed anhydrides of phosphoric acid [88,165–167]. Pyridine can be replaced by isoquinoline; both the yield and the quality of the products diminish with 2-methylpyridine; and no reaction occurs with quinoline.

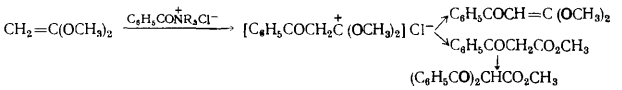
Acyl salts of pyridine and other tertiary amines are able to split off the acyl group under the influence of ethers [168], which resembles the process occurring in alkylpyridinium salts. Thus veratrole, anisole, and diphenyl ether are smoothly decomposed when heated with acylpyridinium chlorides to 220°C, with the formation of esters of the phenols [7]. An interesting preparation of an acyloin has been described, from benzothiazol-2-aldehyde in the presence of acetic anhydride and pyridine, which evidently involves the intermediate *O*-acylation of the *N*-acetylpyridinium ion. Under these conditions chloral forms chloral hydrate diacetate in quantitative yield [169]. The reaction of benzoyl halides with aldehydes in the presence of pyridine has been described [170].

The acylation of amines by acylpyridinium salts is of no great preparative interest, since reactions with acid anhydrides usually proceed satisfactorily even in the absence of a catalyst, but aroylation in pyridine is applicable to amines of enhanced NH acidity [128,129c,130b]. Acylation by acetic anhydride in pyridine is used more widely in the analysis of amines [128,147,150,171,172]. Application of the method to the preparation of sulphonamides has been discussed [173,174]. Both pyridine and triethylamine have an unfavourable effect on the molecular weight of the products in the preparation of polyamides from isophthaloyl and terephthaloyl chlorides and diaminodiphenols [175], which was attributed to catalysis of *NO*-transacylations. The part played by individual *N*-acyl- and *N*-arenesulphonyl-pyridinium salts in the acylation of amines has been discussed [22,39,53,68,76].

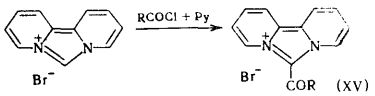
The considerable acylating power of acylpyridinium chlorides is especially clearly developed in reactions

with amides of carboxylic acids: mono- and di-acylation of the amide or dehydration to the nitrile takes place depending on the nature of the acyl halide and the amide [176]. Chlorides of weak acids usually form monoacyl derivatives, those of stronger acids diacylate the amide, and chlorides of strong acids exert only a dehydrating action. For example, 3,5-dinitrobenzoyl chloride in pyridine has been proposed for the quantitative dehydration and hence analysis of amides [128,177]. The reaction goes especially smoothly with benzenesulphonyl and toluenesulphonyl chlorides [145,178]. Sulphonamides can be acylated similarly [179].

Organic compounds can undergo *C*-acylation by acid chlorides in the presence of pyridine, although in most cases the reaction is not regarded as involving initial formation of *N*-acylpyridinium derivatives‡. The action of benzoyl chloride on 1,1-dimethoxyethylene in triethylamine or pyridine, for example, yields a mixture of three products [181]:



Certain nucleophilic heterocyclic nitrogen compounds readily undergo acylation at a carbon atom [182,183]:



The product (XV: R = C_6H_5) can also be obtained by cyclising 1-phenacyl-2-pyrid-2′-ylpyridinium bromide by the action of toluene-*p*-sulphonyl chloride in boiling pyridine [182]. Information has been published on the possible acylation of alkyl groups by certain heterocycles [184,185].

Various β-dioxo-compounds and ketones capable of keto–enol tautomerism generally give *O*-esters—not the *C*-acyl derivatives usually obtained by the acylation of sodium enolates—by the action of *N*-acylpyridinium salts *in situ* [186,187]. Reaction takes place under very mild conditions, sometimes at room temperature or even in the cold. However, Dieckmann et al. [188,189] observed that a *C*-derivative was also present in the acylation of cyanoacetic ester and dihydroresorcinol in pyridine. β-Aminocrotonic ester and its analogues yield *N*-acylated and/or *C*-acylated products depending on the acyl chloride [190]. The use of other tertiary amines generally leads to the formation predominantly of *C*-acylated products [98,181,191,192].

The first attempts to explain the role of pyridine in such reactions were made by Doering and McEwen [98,192,193]. The interaction of benzoyl chloride, pyridine, and acetophenone yielded 1-benzoyl-1,4-dihydro-4-phenacylpyridine (XVI) and *O*-benzoylacetophenone. It was suggested that the *N*-benzoylpyridinium salt attacks acetophenone simultaneously at $C_{(2)}$ and $C_{(4)}$, forming the stable (XVI) and 1-benzoyl-1,2-dihydro-2-phenacylpyridine, which rearranges to the *O*-adduct via a geometrically favourable quasi-six-membered transition state [98,193]. Results of a kinetic investigation of this system were interpreted similarly [194].

Recent results indicate [195,196] that the reaction of acetoacetic ester with benzoyl chloride in pyridine, triethylamine, 2-methylpyridine, and 2,6-dimethylpyridine gives only the *O*-benzoate (but the yield decreases in the above sequence). The reaction is of the first order with respect to both components with inverse proportionality to the chloride-ion concentration. All reactions are slower in non-polar solvents. Acylation is assumed to proceed via the keto-form of acetoacetic ester without involving intermediate products of addition to the pyridine ring; in the case of benzoylation the slow stage is formation of a benzoylammonium salt, which is hindered when the nitrogen atom is shielded. Further research is obviously necessary before a final solution will be obtained to the problem of the mechanism of the *O*-acylation of β-keto-enols.

2. Nucleophilic and General Base Catalysis by Pyridine Bases

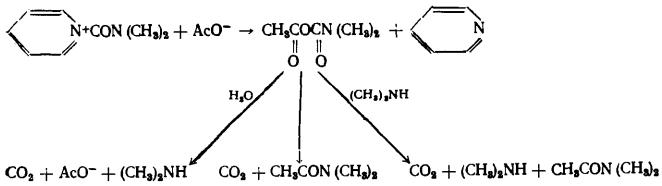
The study of reactions involving the migration of an acyl or a phosphoryl group in systems comprising an *N*-acylpyridinium ion and a nucleophile not only has enabled the kinetic and thermodynamic factors governing the stability of salts of *N*-acylated heterocyclic cations to be estimated (although such data are still too few), and the influence of structural and steric factors in nucleophilic reagents on their reactivity to be assessed, but has also introduced some clarity into our understanding of the mechanisms of nucleophilic reactions and certain problems of nucleophilic catalysis [137–139]. Furthermore, *trans*-acylations and *trans*-phosphorylations are directly involved in problems of biochemistry and bio-organic chemistry [137,138,197].

Nucleophilic catalysis implies attack by a nucleophile on a substrate (ester, anhydride, acid chloride), leading to the formation of an unstable intermediate structure, which then breaks down either spontaneously, catalytically, or under the influence of a weaker nucleophile to give the final product and regenerate the catalyst. General base catalysis covers the exchange of a proton between a base and a substrate at the rate-determining stage of a reaction. The former type of catalysis is regarded as typical of acid derivatives having a "good" leaving group (halide, acetate, radical of an alcohol of high pK_a) [198–200], and the latter of so called inactivated esters [198]. Among tertiary amines nucleophilic catalysis is typical of pyridine, its 3- and 4-methyl (polymethyl) derivatives, and isoquinoline; 2-methyl derivatives of these heterocycles and often quinoline itself are weak catalysts, despite their high basicity, because of steric hindrance of the nitrogen atom. The applicability of Brønsted's relation between lg k_B and pK_a to pyridines substituted at all positions in the ring is usually interpreted as evidence of general base catalysis [139]. The isotope effect on passing from water to deuterium oxide as solvent is $k_H/k_D = 2–3$ for most reactions, including acid–base equilibrium, and is close to unity for the nucleophilic hydrolysis of derivatives of organic acids [201–204].

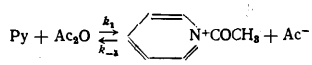
N-Dimethylcarbamoylpyridinium chloride (V) is stable in acidified aqueous solutions (pH 1–5), but undergoes rapid decomposition catalysed by the hydroxide ion when the solution is made alkaline [102]. On the addition of hydroxylamine hydrochloride, imidazole, sodium azide, sodium fluoride, or the formate ion, direct nucleophilic

‡The Dakin–West reaction involves *C*-acylation at an intermediate stage [180].

substitution occurs at the nitrogen atom. Hydrolysis of (V) is accelerated also by components of the buffer solution (e.g. the acetate ion):



Comparing the behaviour in aqueous solutions of solid *N*-acetylpyridinium chloride and of systems formed by acetic anhydride with pyridine bases, Jencks and Fersht [20,110,205] conclude that appreciable quantities of the *N*-acylpyridinium and its homologues may accumulate in aqueous buffer solutions. Increasing the concentration of the acetate ion lowers the quantity of acetylpyridinium formed by raising the rate k_{-1} of the reverse reaction. Pyridine has the opposite effect:



4-Substituted pyridines show a dependence on the basicity of the nitrogen atom (Table): the quantities lg k_1 and lg K_{eq} correlate satisfactorily with pK_a of the base.

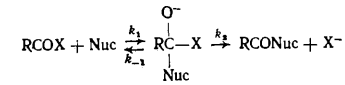
Relations between structure and reactivity in *N*-acetylpyridinium ions [20].

Base	pK_a of base	k_1, mole^{-1} s^{-1}	K_{eq}	Hydrolysis rate const. k_2, mole^{-1} s^{-1}		$-\Delta F^{\neq}$ of hydrolysis
				water	acetate ion	
Pyridine	5.51	84	0.092	6.9	910	18.31
4-Methylpyridine	6.33	490	1.86	2.3	262	17.67
3,4-Dimethylpyridine	6.79	1160	9.67	1.5	120	17.33
4-Methoxypyridine	6.82	935	31.2	0.4	30	16.65
Imidazole	—	—	2950	—	—	14.05

The acetylation of anisidine and *p*-toluidine by acetic anhydride in the presence of pyridine in aqueous solution is pseudo-unimolecular, with a rate constant independent of the type or concentration of arylamine. Hence the migration of an acyl group passes through a limiting stage in which the acetylpyridinium ion is formed, followed by rapid reaction with the nucleophile [20,110]. Thus these amines at concentrations of $(5–10) \times 10^{-4}$ M compete successfully with water, which illustrates the high selectivity of acetylpyridinium ions for the type of nucleophilic agent [20,206–208]. Corresponding comparative data for water and acetate ions (Table) are well correlated by Brønsted's equation ($\beta = -0.5$ and 0.68 respectively).

Values of k_2 for the nucleophilic substitution of the four *N*-acetylpyridinium ions in the Table with thirteen *O*- and *N*-nucleophiles (alkoxide and phenoxide ions, aliphatic amines, cyclic amines, and hydrazines) reveal a decrease in sensitivity ("levelling") of the acetylpyridinium ions to the basicity of the attacking nucleophile as this quantity increases [205]. The Brønsted constants fall in a series of *O*-nucleophilic reagents, from 0.9 for the acetate ion to 0.2 in alkoxides. For amines of moderate strength $\beta = 0.9$, after which it drops sharply. "Levelling" is absent in the less reactive acetylimidazolium ion.

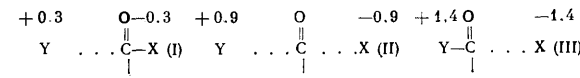
The scheme which has now been worked out for reactions at the carbonyl group in derivatives of carboxylic acids postulates the equilibrium formation of a tetrahedral addition product, which then breaks down:



(Nuc = neutral molecule or anion)

With strongly basic nucleophiles the intermediate adduct is rapidly converted into the final products, and when $k_2 \gg k_1$ the addition stage (k_1) is rate-determining. The dependence of the reactivity of the acid derivative RCOX on the basicity of the leaving group X will then be minimal. With weaker nucleophiles k_{-1} is relatively larger, and cleavage of the adduct begins to limit the overall rate of the process. Bender demonstrated that the second stage could rightly be chosen as determining the rates of reactions involving inactivated esters [137,138]. These concepts are often used also to explain the regular features of nucleophilic substitution at a quinquevalent phosphorus atom. However, isolated reactions may occur at the carbonyl group and at the phosphorus atom without necessarily involving intermediate formation of addition products.

Jencks [205,208] has proposed a new classification of acyl migrations, which depends on the strength of the nucleophile and on the values of β for the nucleophile and for the leaving group:



(the numbers denote the change in the charge on the attacking or leaving group of atoms compared with the change of 1.7 for the complete reaction). The first class comprises reactions of strongly basic nucleophilic reagents with acylating compounds having good leaving groups (i.e. with *N*-acetylpyridinium ions); they have an unsymmetrical transition state with relatively little formation of new bonds and destruction of old bonds (termed an early transition state). These reactions bear a definite resemblance to S_N2 substitutions at a saturated carbon atom.

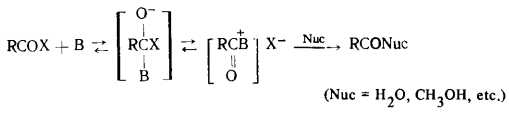
The third class, on the other hand, includes reactions of feebly basic nucleophilic reagents and compounds with poor component groups. If the existence of an intermediate tetrahedral adduct is assumed, its cleavage determines the overall rate of the reaction. The second class covers many reactions where the transition state is more or less symmetrical with respect to the attacking and leaving groups ($\beta = 0.7–1.0$). It includes also reactions of acetylpyridinium ions with amines where the two groups have closely similar pK_a values. Formation of a tetrahedral intermediate structure is difficult to predict here.

The aminolysis of 4-substituted *N*-phosphorylpyridinium ions (XI) in aqueous solution by aliphatic and heterocyclic amines and imines having pK_a = 2.6–10.8 shows slight sensitivity to the basicity of the attacking group (Brønsted nucleophilic constant in the range 0.2–0.3) [86]. The value of k_2 for the nucleophilic reagent is strongly dependent on the nature of the leaving group in (XI).

Information has been published on the hydrolytic stability of several other solid *N*-phosphorylpyridinium salts and their *N*-acyl analogues [25,30,31,68,86,110]. In both series

the rate of hydrolysis decreases with increase in the basicity of the 4-substituent, as a consequence of delocalisation of the positive charge through the longer conjugated chain. The contribution of onium or immonium forms should, of course, increase in the sequence $\overset{+}{H}O=$, $\overset{+}{N}H_2=$, $R\overset{+}{N}H=$, $R_2\overset{+}{N}=$. In conformity with this the resonance-stabilised 1-acetyl-4-dimethylaminopyridinium chloride is hydrolysed more slowly than the unsubstituted *N*-acetylpyridinium chloride with a rate ratio of 1/2000.

Nucleophilic catalysis by pyridine bases has been proved for the hydrolysis of acetic anhydride (in water [113,209], an acetate buffer [206,210,211], and aqueous-organic mixtures [199,212,213]), several mixed anhydrides [113,214], various acid chlorides in 89% aqueous acetone [99], acetyl fluoride [207], and arenesulphonyl chlorides in water [215]. Another model in kinetic investigations of hydrolysis is provided by *p*-nitro- and 2,4-dinitro-phenyl acetates [216-218], and certain sulphonic esters [219-221]. Nucleophilic catalysis by various pyridine derivatives of the methanolysis of 2,4-dinitrophenyl acetate, picryl acetate, and picryl benzoate, certain enol acetates, and arenesulphonyl chlorides has been investigated [222-227]. In all cases the results agree satisfactorily with the general scheme of catalysis



(Nuc = H_2O, CH_3OH, etc.)

The hydrolysis of acetic anhydride is highly sensitive to the acetate-ion concentration [206,210,211,213]: e.g. the catalytic effect of pyridine is completely inhibited in the presence of a buffer comprising 1.06 M acetate plus 0.54 M acetic acid in 40% dioxan [206]. On the other hand, the extraordinarily high isotope effect of $k_{H_2O}/k_{D_2O} = 5 \pm 1$ has been found for hydrolysis in acetate buffers [210,211]. This could be explained theoretically on the assumption of solvolysis of the acetylpyridinium ion as the rate-determining stage [201-203].

Transfer from water to methanol as solvent slows down the solvolysis of acetic anhydride by a factor of 10^5 [219], and in the latter solvent pyridine is only slightly more active than the acetate ion as a catalyst. Hydrolysis catalysed by pyridine is retarded with increase in the concentration of dioxan in mixtures with water [206,213]; it is supposed that decrease in the polarity of the solvent is accompanied by a significant fall in the equilibrium constant K_{eq} of the stage of formation of the *N*-acetylpyridinium ion (decrease in k_1 with simultaneous increase in k_{-1}).

Study of the hydrolysis of several chlorides of carboxylic acids in 89% acetone in the presence of butylamine, trimethylamine, triethylamine, pyridine, and trimethylpyridine distinguished [99] those reacting by an S_N2 mechanism (through formation of *N*-acyl salts) from those reacting by unimolecular ionisation (S_N1). The rates of hydrolysis of piperidinocarbonyl, *NN*-di-isopropylcarbamoyl, and 2,4,6-trimethylbenzoyl chlorides remained almost unchanged in the presence of any of the amines, but acetyl, pivaloyl, benzoyl, and 2,4,6-trimethyl-3,5-dinitrobenzoyl chlorides showed a 10^5–10^7-fold acceleration in the presence of pyridine. The sequence of catalytic activity obtained for the tertiary amines

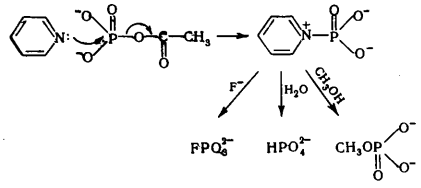
pyridine > trimethylamine > triethylamine > trimethylpyridine

is typical of nucleophilic catalysis.

The hydrolysis of benzenesulphonyl chloride in aqueous solution in the presence of ten pyridine derivatives having donor and acceptor substituents at positions 3 and 4 in the ring is well represented by the first-order equation $k_{obs} = k_w + k_b[B]$ [215,227]. The reaction is accelerated by the presence of donor substituents, and slowed down by acceptor substituents. Its sensitivity to the basicity of the nucleophiles is intermediate between the above cases of carbonyl compounds and phosphoric acids. It is postulated that, because of the greater polarisability of the sulphur atom, the bond may be formed in the transition state at a greater distance than for the carbon atom.

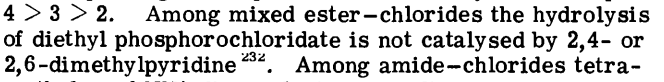
Various acid derivatives of phosphorus are of considerable interest in connection with the factors governing the possibility that hydrolysis may occur by mechanisms of general base and nucleophilic catalysis [197,228]. The relative reactivity of substrates may be affected not only by structural features but also by the pH of the solution (neutral molecule, mono- and di-anion).

In 1952 Koshland discovered that pyridine catalyses the hydrolysis of an acetyl phosphate in buffer solutions [19]. The list of nucleophilic catalysts was later extended when it was established that pyridine, 4-methylpyridine, triethylenediamine, and probably triethylamine attack the phosphorus atom preferentially, ensuring rupture of the phosphorus–oxygen bond, whereas trimethylamine, imidazole, and *N*-methylimidazole cause rupture of the carbon–oxygen bond [229,230]. The reactions were not catalysed by 2-methylpyridine, 2,6-dimethylpyridine, or 2,4,6-trimethylpyridine, which is consistent with the scheme



In the case of acetyl phenyl phosphate all the amines mentioned attack only the carbon atom, being catalysts of acyl migration.

Di-isopropyl and diethyl phosphorofluoridates are hydrolysed in a bicarbonate buffer 5–20 times as rapidly in the presence of 10 mole % of imidazole and pyridine derivatives [231]; with picolines the catalytic activity diminishes depending on the position of the methyl in the sequence 4 > 3 > 2. Among mixed ester–chlorides the hydrolysis of diethyl phosphorochloridate is not catalysed by 2,4- or 2,6-dimethylpyridine [232]. Among amide–chlorides tetramethyl- and *NN'*-dipropyl-phosphorodiamidic chlorides are hydrolysed at comparable rates in neutral or weakly acid aqueous solutions, the reactions being catalysed by 3,5-dimethylpyridine, pyridine, and 4-methylpyridine, but not by their 2-methyl analogues [200]. On the other hand, some catalysis by 2,6-dimethylpyridine has been found with *NN'*-diethylphosphorodiamidic chloride (XVII), obviously by the general base mechanism [232]:



Nucleophilic catalysis has been established for hydrolysis of the phosphorus-nitrogen bond in phosphoramidic [233-235] and *p*-chlorophenylphosphoramidic [236] acids. In neither case did 2-methylpyridine, 2,6-dimethylpyridine, or pyridine-2-carboxylic acid show appreciable activity. A test of six pyridine bases having $pK_a = 2.8$–6.0 gave satisfactory correlation of the Brønsted k_2 values ($\beta = 0.22$) [235]: i.e. the anions of these amides exhibit the same

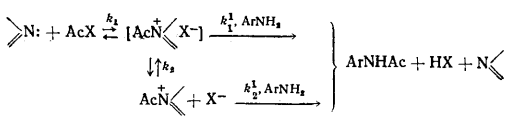
diminished sensitivity to the basicity of the nucleophile as does N-phosphorylpyridinium (XI)[86]. It was proved that intermediate N-phosphorylated pyridines may accumulate during the reaction.

A similar pattern of nucleophilic catalysis is exhibited by the hydrolysis of the dianions of *o*- and *p*-nitrophenyl phosphates substituted in the ring by hydrogen, chlorine, acetyl, and nitro[237-239]. In the last case the reaction with pyridine is highly sensitive to the leaving group ($\rho = -1.03$), and almost completely insensitive to the basicity of the attacking group. This probably belongs to the first type of nucleophilic reactions in the Jencks classification[205], with almost complete absence of a phosphorus–nucleophile bond in the transition state. Pyridine bases and other nitrogen nucleophiles do not catalyse the hydrolysis of monoanions of phenyl, *p*-nitrophenyl, and *o*-nitrophenyl phosphates[236,238], but acceleration has been found with *para*-substituted *o*-nitrophenyl phosphates[238]. The reaction mechanism is assumed to approximate to the classical $S_N2(F)$, with formation of new bonds and rupture of old bonds in the transition state (type II in the Jencks classification).

Among neutral phosphoric esters appreciable catalysis by pyridine derivatives and imidazole has been found with ethylene methyl phosphate[240]. In buffer solutions ring-opening takes place preferentially, and to a less extent hydrolysis of the P–OCH_3 bond. The reaction is only slightly affected by steric hindrance in the catalyst molecule (4-methylpyridine > 3-methylpyridine > 2,4-dimethylpyridine > pyridine > 2,6-dimethylpyridine) and has $k_{H_2O}/k_{D_2O} \simeq 2$. Hence it is an example of general base catalysis. Tetrabenzyl pyrophosphate has also been investigated[241,242].

Litvinenko and his coworkers[243-253] have made a long series of kinetic investigations on the benzoylation of arylamines in the presence of tertiary amines in aprotic solvents. Various substituted pyridines exhibit high catalytic activity, considerably exceeding those of triethylamine and dimethylaniline[243,244]. The sequence of relative efficiencies follows the increase in basicity (pK_a in water) of the pyridine base: 3-NO_2 < 3-Cl < H < 3-CH_3 < < 4-CH_3 < 4-$(CH_3)_2N$. The Hammett correlation gives $\rho = -3.74$, indicating that the catalytic effect is highly sensitive to structural changes in the catalyst; 2-methylpyridine and 2,6-dimethylpyridine are relatively ineffective. A similar correlation was made of the constants of the non-catalytic reaction k_0 and of the catalytic reaction k_B with respect to the structure of the arylamine $RC_6H_4NH_2$ ($\rho = -2.67$, -1.35): this corresponds to an increase in the effective charge on the reaction centre in the transition state for catalysis by pyridines. The ratio k_B/k_0 increases as the amine to be acylated becomes less strongly basic, which is typical of nucleophilic reactions. The influence of *meta*- and *para*-substituents in the benzoyl chlorides is less marked, and *p*-chloro-, *p*-methoxy-, and *p*-dimethylamino-benzoyl chlorides are appreciably less reactive than would be expected from the σ-values. It has been explained by postulating the possibility of direct polar conjugation of the substituents with the reaction centre, which is more strongly developed than in Hammett's standard series (dissociation of carboxylic acids[248]).

Kinetic confirmation has recently been obtained of the formation of N-acyl salts during the acylation of *p*-anisidine by *m*-toluene- and *p*-nitrobenzene-sulphonyl chlorides in nitrobenzene in the presence of pyridine[252,253]. Values of $k_{eff} = k_0 + k_{Py}[Py]$ fell as the reaction proceeded. This is possible if the intermediate adduct of pyridine with the arenesulphonyl halide (acyl halide) dissociates into ions, either partly or completely, in the strongly ionising solvent, so that two catalytic paths—interaction of the arylamine with an ion-pair or with an acylpyridinium cation—are available for the reaction. Accumulation of the gegenion (Br^-, Cl^-) will displace the dissociation equilibrium and then formation of the primary adduct, similarly to the hydrolysis of acetic anhydride and phenyl acetates[206,208]:



(for cases of acylation by means of acid anhydrides see Refs. 245 and 250).

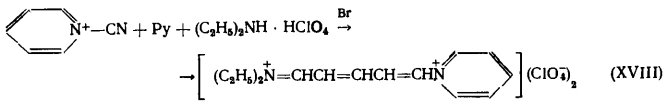
Bonner and his coworkers[116,254,255] have recently studied the kinetics of the trifluoroacetylation and the acetylation of several phenols and alcohols by trifluoroacetic, acetic, and trifluoroacetylacetic anhydrides in the presence of pyridine and its homologues in carbon-tetrachloride solution. The pyridines are assumed to have a dual function: they form hydrogen-bonded solvates with phenols, which makes the oxygen atom more strongly nucleophilic; and they solvate the leaving acetoxy-group in the transition state[116]. Calculation showed[254] that the hydrogen bonding of *p*-cresol and *p*-chlorophenol makes them more strongly nucleophilic by factors of 300 and 700 respectively. The degree of association of aliphatic alcohols with pyridines is small, which explains the slight catalytic effect (at 25°C). The isotope effects $k_H/k_D = 1.51$ and 1.40 obtained with deuterophenol and duetero-*p*-chlorophenol indicate that heterolysis of the oxygen–hydrogen bond is of some importance in acetylations[255].

Korshak et al.[105,256-259], in an investigation of low-temperature polyesterification in the presence of tertiary amines, also conclude that two mechanisms of catalysis—nucleophilic and general base—operate in the acylation of monohydric and dihydric phenols by acid chlorides. The latter mechanism is especially important with highly basic aliphatic amines (e.g. triethylamine) and highly acidic phenols[256]. Nucleophilic catalysis evidently predominates with sterically unhindered pyridine bases[257]. Thus the degree of conversion of phenol in the competitive benzoylation of phenol and methanol fell rapidly as pK_a decreased in the series of bases—tributylamine, triethylamine, ethyldimethylamine, 2,4,6-trimethylpyridine, 2-methylquinoline, 2-methylpyridine, isoquinoline, 3-methylpyridine, pyridine, and quinoline[258]. The solvent—its tendency to solvate the reactants physically and chemically—has an appreciable effect on the relative contributions of nucleophilic and general base catalysis. The quantity $q = (1 - x)/x$, where x is the conversion of phenol, has maximum values in dioxan, acetone, and nitrobenzene, and minimum values in benzene and dichloroethane.

3. Reactions of N-Acylpyridinium Cations with Opening of the Ring

Cleavage of the pyridine ring (the Zincke–König reaction[3,119-141]) with the formation of glutaconaldehyde or its anils or enamines is characteristic of quaternary pyridinium and benzopyridinium salts containing an electron-accepting substituent attached to the nitrogen atom. N-(2,4-Dinitrophenyl)- and N-cyano-pyridinium salts are cleaved in this way in the presence of alkali and various

aromatic amines and *N*-alkylanilines[260–265]. 4-Methylpyridine and 4,4'-bipyridyl have also been used successfully (but not 2-methylpyridine). Besides the use of cyanogen chloride and bromide, the König reaction has been accomplished by the action of sulphur trioxide and ethyl chlorosulphate[226], carbonyl chloride, phosphoryl chloride, phosphorus pentachloride, thiocarbonyl chloride, and other thio-acid chlorides[262,267]. The combined action of cyanogen bromide and triethylamine perchlorate on pyridine yields the simplest polymethine dye (XVIII)[268]:

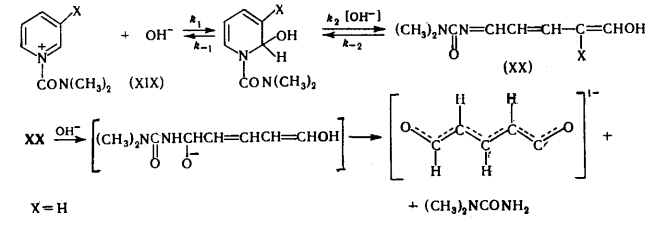


(XVIII)

The view arose (probably because of the predominance of acylation processes) that acyl chlorides were incapable of initiating cleavage of the pyridine ring[262,269]. However, such a process was observed on the interaction of diphenylcarbamoyl chloride with pyridine in the presence of alkali[40] and when adducts of pyridine with di-*o*-tolyloxalimidoyl chloride and with *N*-phenylbenzimidoyl chloride were treated with various aromatic amines in alcoholic solution[45]. A case in which alkaline benzoyl chloride was used was also reported[270], but the yield of glutaconaldehyde was not indicated. Derivatives of this aldehyde are obtained in almost theoretical yield when *N*-nitro- and *N*-nitroso-pyridinium ions are cleaved under alkaline conditions[119,270]. This reaction is a sensitive test for pyridine[74,271]. Other analytical applications of the König reaction will be found in Refs. 272–276.

The cleavage of *N*-acylpyridinium salts is facilitated by the presence of compounds containing active methyl or methylene groups. They condense with the cleavage product to give polymethine dyes. Thus aroyl chlorides and pyridine react comparatively readily with 2,3-dihydro-2-oxobenzofuran, oxindole, or 3-hydroxy-1-methylindole[63,277]. With cyanoacetic esters initial nucleophilic addition to acylpyridinium salts is followed by opening of the pyridine ring at $C_{(2)}$[278].

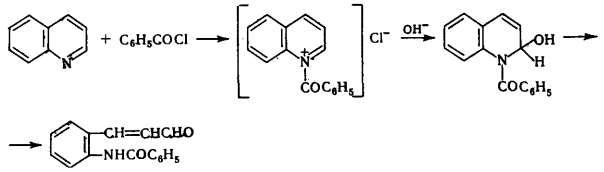
Kinetic investigation of the cleavage of *N*-dimethylcarbamoylpyridinium cations (XIX: X = H, $CONH_2$) under alkaline conditions[44,279,280] shows that the equilibrium formation of pseudobases when the hydroxide ion attacks the ring at $C_{(2)}$ is more rapid than opening of the ring. The rate of the latter is proportional to $[OH^-]^2$ or $[B][OH^-]$, where B is a base (e.g. CO_3^{2-}). The resulting 5-dimethylureidopenta-2,4-dienals (XX)



X = H

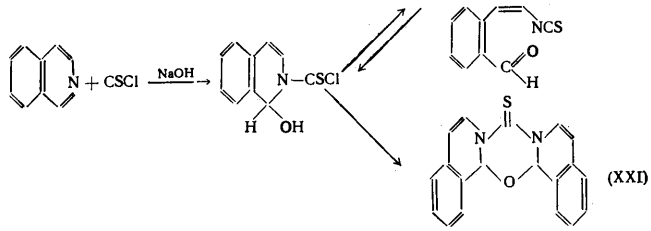
are relatively stable, and can be isolated from the solution. The strong "acidifying" action of the 3-carbamoyl group in (XIX) on the relative ease of formation of the pseudobase is significant: the pH of equilibrium between cyclic and open-chain forms is shifted to 8.6 from 10.64 for X = H; the constants $k_2(CONH_2)$ and $k_2(H)$ differ by factors of 10^5, although for reactions involving migration of the acyl group (Section III, 2) they increase only 3 to 14 times[44].

N-Alkyl-quinolinium and -isoquinolinium pseudobases are very stable and exist only in the cyclic form[4]. For this reason Reissert assigned a pseudobase structure to the product of the reaction of quinoline with benzoyl chloride in the presence of 10% alkali[34], but later he suggested the "open" benzamidocinnamaldehyde structure[281]:



The open structure (with the *trans*-configuration) has now been proved by various spectral methods[282,283].

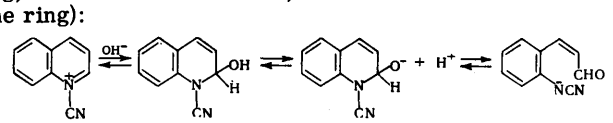
Reissert's method is of applied significance for the preparation of various polyfunctional compounds[282]. Pseudobases can be prepared by means of cyanogen bromide[284–287]. Reaction of isoquinoline with thiocarbonyl chloride in alkaline medium yields a ring-cleavage product together with a compound (XXI) formed by dehydration of the pseudobase[288]:



(XXI)

A stable pseudobase has been obtained from an *N*-benzoyl salt of 5-nitroquinoline; in this case its cyclic structure and the absence of tautomeric conversion to an acyclic form have been proved[283].

A series of studies by Johnson and his coworkers[106,123,126,283,287–290] on *N*-cyano-quinolinium and -isoquinolinium ions have revealed the great importance of pseudobases in the occurrence of most reactions of such compounds (acid–base equilibria of two types, hydrolysis, ring-opening, formation of *O*-ethers, bromination and nitration in the ring):



The formation of pseudobases and opening of the pyridine ring are two stages of a general process of attack by the nucleophilic reagent (hydroxide ions, arylamines) at the α-carbon atom of the heterocyclic ring. This process frequently competes with reactions involving migration of the acyl group to other nucleophiles.

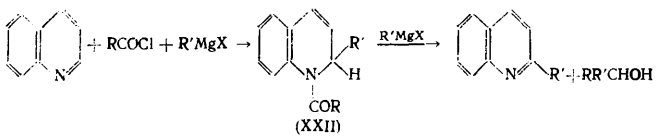
4. Hetarylation

The reaction of *N*-acyl-quinolinium and -isoquinolinium salts with the cyanide ion is of great importance for synthetic organic chemistry. In contrast to the hydroxide ion, the cyanide ion does not cleave the heterocyclic ring and, with few exceptions, does not detach the acyl group. Attack at $C_{(2)}$ leads in this case to the formation of extremely stable 1-acyl-2-cyano-1,2-dihydroquinolines or 2-acyl-1-cyano-1,2-dihydroisoquinolines (so called

Reissert compounds). *N*-Acyl-pyridinium and -acridinium salts do not undergo this reaction[34,281]—see, however, Ref. 291. In view of the appearance of two reviews on the Reissert reaction[292,293], we shall merely give references to the most important papers published during the past three years on the subject of the present paper[294-310]. The interaction of *N*-cyanoquinolinium with anhydrous hydrogen cyanide has been discussed[283,284].

Pyridine undergoes the Grignard reaction with difficulty, while its *N*-alkyl salts are sparingly soluble in most of the solvents used in this synthesis[1]. When pyridine interacts with a Grignard reagent in the presence of acylating agents, the corresponding 1,4-dihydropyridines are formed[292], and easily pass into 4-substituted pyridines. With 4-substituted pyridines, however, Grignard reagents attack position 2, not 4, in the *N*-acylpyridinium ions[311].

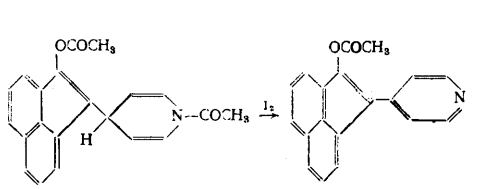
The addition of Grignard reagents to a mixture of quinoline and an acyl halide gives compounds of type (XXII), but with the reactants mixed in the opposite sequence, i.e. in excess of the organomagnesium compound, the 1,2-dihydro-derivative loses a proton, and is converted into a 2-substituted quinoline[312,313], the acyl group giving the corresponding tertiary alcohol:



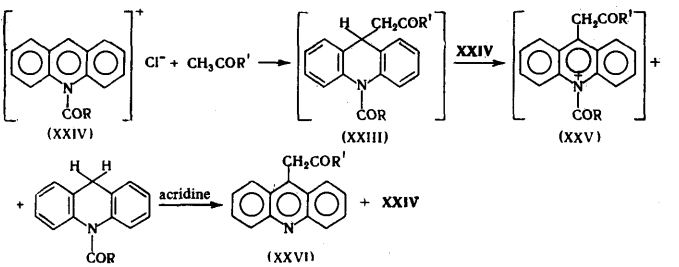
(XXII)

Similarly, *N*-acylpyridinium salts react *in situ* with silver acetylides at position 2[314].

In the early work Claisen and Haase[315], in a study of the reaction of acetophenone with benzoyl chloride in the presence of pyridine, isolated a compound $C_{20}H_{17}NO_2$ as well as the expected *O*-benzoyl derivative of the enol. Much later a compound containing a pyridine group was also obtained by the acylation of acenaphthenone with acetic anhydride in pyridine[316]. McEwen[98] showed that 4-substituted 1-acyl-1,4-dihydropyridines had been obtained in both cases: e.g. Ghigi's product[316] was 2-(1-acetyl-1,4-dihydropyrid-4-yl)acenaphthylen-1-yl acetate. Oxidation by iodine gives the 4-substituted pyridine:



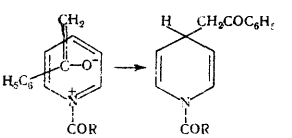
Under similar conditions *N*-acylquinolinium salts usually "quinolinate" both monocarbonyl and β-dicarbonyl compounds to form 2-substituted 1-acyl-1,2-dihydroquinolines[192,278]. Hetarylation—not acylation—products also constitute the main yield of the reactions of *N*-acylated isoquinolinium, phenanthridinium, and acridinium salts with various keto-compounds[317,318]. In this way preparative yields of ketones of the acridine series have been obtained directly from acridine and acyl halides with acetophenone. The probable mechanism of the latter reaction is that the initially formed 10-acyl-9,10-dihydro-9-phenacylacridine (XXIII) is converted, by detachment of a hydride ion on attack by an *N*-acylacridinium cation, into an unstable *N*-acyl salt (XXV), which is decomposed by excess of acridine with regeneration of the salt (XXIV) and formation of the product (XXVI)[319]:



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

The distribution of electron density can be used to explain preferential attack by a nucleophile at position 2 or 4 in the pyridine ring[320]. Other approaches have tried to take into account both the electronic nature of the two reactants and the character of the transition state (Kosower–Klopman theory[321,322] and Pearson's general acid–base principle[323]).

Kosower[324] suggested that substitution occurs at the $C_{(4)}$ atom of the pyridine ring if the reagents (electron donors) form charge-transfer complexes with pyridinium cations; if, however, the formation of such complexes is hindered, position 2 is substituted. For example[321], the benzoylpyridinium cation reacts with the enolate anion of acetophenone to form initially an adduct (XXVII), in which the nucleophilic atom of the ambident group is situated near position 4, and the anionic centre near the positively charged nitrogen atom:

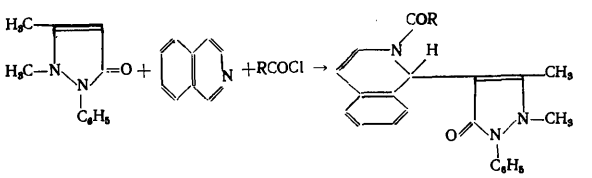


(XXVII)

Nevertheless, Kosower himself stresses that his ideas do not apply to the behaviour of the cyanide ion, which attacks *N*-alkylpyridinium salts solely at $C_{(4)}$, although no absorption band corresponding to charge transfer has yet been detected.

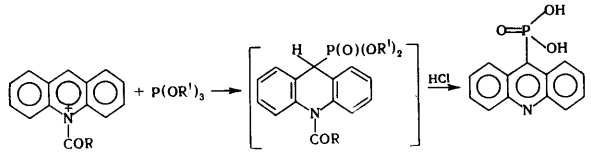
In terms of Pearson's generalised acid–base principle[323] the character of the attack by the nucleophilic agent (a generalised Lewis base) on *N*-acylated heteroaromatic cations, which are ambident ions, will be determined by the relative "hardness" or "softness" of individual positions in the ring. Hence position 4 is attacked in pyridinium salts, but the orientation in quinoline and isoquinoline remains obscure as before. The thermodynamic factor is probably decisive[122,325]. Comparison of the 1,2- and 1,4-dihydroquinoline structures shows the former to be thermodynamically preferred, with the $C_{(3)}=C_{(4)}$ double bond conjugated with the benzene ring, and the necessary conditions established for production of a homoaromatic structure (in terms of Winstein's ideas[326]).

The reactions of *N*-acylated heterocyclic cations *in situ* with pyrazolones, thiazolidine-2,4-diones, rhodanine, thio- and iso-rhodanines, azalactones, and other azolidones are of the same type (interaction with ambident methine anions)[327-331]:

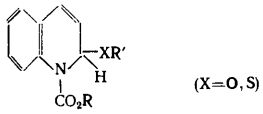


It has recently been established that the Dakin–West synthesis involves the intermediate pyridylation of oxazolones by *N*-acetylpyridinium cations [332,333] (for greater detail see Ref. 180). The cyclopentadienyl ring has also been hetarylated (by the reaction of *N*-acylated pyridinium and benzopyridinium salts with azulenes) [334]. The reaction of *N*-acylpyridinium salts with nitroalkanes [335] yields anomalous products not containing a pyridine ring, but quinolinium salts form hetarylation products containing two quinoline ring systems.

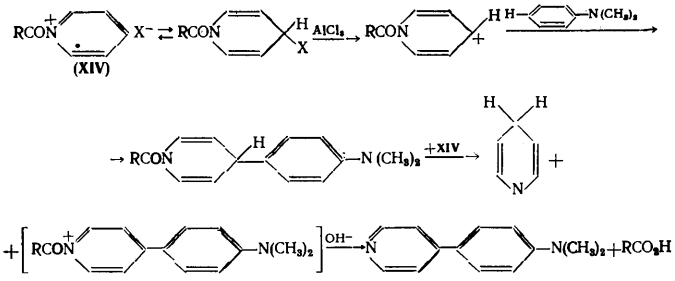
Interaction between *N*-acylated heteroaromatic cations and compounds having a heteroatom with a lone pair of electrons mostly involves attack on the carbonyl carbon atom, as stated above, with elimination of the heterocycle and migration of the acyl (acylation of amines, alcohols, thiols, etc.). However, there are several examples of reactions occurring by a mechanism of hetarylation. Thus the well known synthesis of *N*-pyrid-4′-ylpyridinium chloride by chlorinating pyridine with thionyl chloride [336–338] probably involves attack by pyridine as a nucleophile on $C_{(4)}$ in the *N*-acyl salt. Among the very few cases of intramolecular hetarylation is the formation of dyes by interaction between quinoline-2-carboxylic acid and acetic anhydride or between quinoline-2-carbonyl chloride and quinoline [339–341]. Another example is the successful accomplishment of the Arbuzov rearrangement for trialkyl phosphites by the action of *N*-acyl-pyridinium, -quinolinium, and -acridinium salts [342,343]:



It has recently been shown [344] that, in the presence of acylating agents (ethyl chlorocarbonate, acetyl and benzoyl chlorides), quinoline readily adds alkoxide and thiolate ions at position 2. This method has been used to prepare high yields of 1,2-dihydro-derivatives of general formula

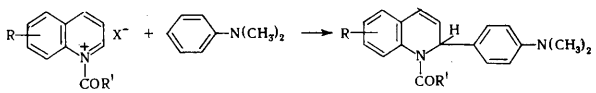


During recent years the chemistry of *N*-acylpyridinium salts has been developed most widely in the hetarylation of the aromatic ring. Like the usual inorganic cations and the widely studied carbonium ions, acylpyridinium ions and their benzo-analogues have proved convenient reagents for the introduction of a heteroaromatic substituent into an aromatic ring§. *N*-Benzoylpyridinium chloride is mostly used in the presence of aluminium chloride or copper powder [112,345,347], when there is no need to isolate the *N*-acylpyridinium salt. The mechanism of the reaction is apparently that the positive charge on the pyridine cation, as a result of the action of the aluminium chloride, becomes concentrated on the 4-carbon atom to form a carbonium ion:



It may also be supposed that *N*-acylpyridinium halides are present in solution either as charge-transfer complexes or as ion-pairs, in which donor–acceptor interaction occurs between the pyridinium cation and the anion [324]. Such systems are less strongly electrophilic than the "purer" cations present in salts with weakly nucleophilic anions like perchlorate, tetrachloroaluminate, etc. This is another explanation of the action of Lewis acids. In a comparative series of experiments on the pyridylation of dimethylaniline with various aliphatic acid chlorides the yield of 4-*p*-dimethylaminophenylpyridine increased as the alkyl chain became longer, which is evidently connected with the strengthening of the electron-accepting effect of the *N*-substituent in the intermediate *N*-acyl salt [37].

N-Acylquinolinium salts, which are most strongly electrophilic, react with dialkylanilines and their analogues in the absence of catalysts [351,352]:

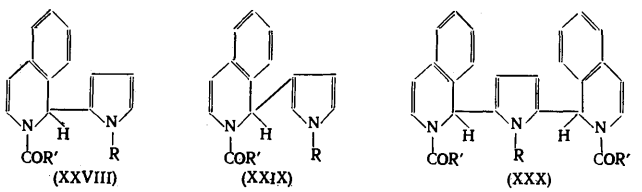


The nature of the anion in *N*-acylquinolinium salts has a significant effect on the yield of quinolination products. Thus the yield of 1-benzoyl-2-*p*-dimethylaminophenyl-1,2-dihydroquinoline increased regularly in the reactions of dimethylaniline with quinoline and a benzoyl halide (fluoride, chloride, bromide, iodide), which may be attributed simply to the increasing reactivity of the benzoyl halides in this sequence. On the other hand, this effect can also be explained by the formation of charge-transfer complexes (with transfer of the electron of the anion to a non-bonding orbital of the heterocycle), which facilitates occurrence of the reaction by a radical mechanism. The possibility of a radical scheme is seen still more clearly in the hetarylation of dialkylanilines by *N*-acylisoquinolinium salts [353,354], since the yields of reaction products were increased by exposure to ultraviolet radiation. The reaction between dialkylanilines and phenanthridinium salts proceeds similarly, but with smaller yields [355].

Acridine reacts more vigorously than other benzopyridines with dialkylanilines in the presence of acylating agents, but it forms 9-arylacridines and *N*-acylacridans [356], not 10-acyl-9-aryl-9,10-dihydroacridines. Hetarylation by acylpyridinium or acylbenzopyridinium salts has been described also with 1-alkyl-2,3-dihydroindoles, *N*-alkyltetrahydroquinolines, *N*-phenylmorpholine, *N*-phenylpyrrolidine, etc. [354,355,357–364]. Similarly to the benzene ring, acylpyridinium cations readily attack the electron-excess rings of such heterocycles as pyrrole, furan, and indole.

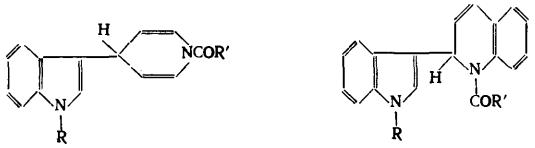
§Some 10–15 years ago there were only isolated publications on this topic [17,345,346]. After pyridylation had been developed [112,347], however, many papers appeared on hetarylation by quinolinium [348], pyrylium [348–350], etc. salts.

Fischer [365] long ago isolated a pyridine-containing substance from the action of pyridine and cyanogen bromide on ethyl 2,4-dimethylpyrrole-3-carboxylate. Much later pyrrolylpyridine derivatives of undetermined structure were obtained.[366,367] by the acylation of pyrroles with acyl chlorides in pyridine solution. However, a more detailed study of the reactions of *N*-acylpyridinium salts and the corresponding benzo-analogues with pyrroles has been made only comparatively recently[368-377], and has shown the formation of both monoadducts (of types XXVIII and XXIX) and bisadducts (XXX).



(XXVIII) (XXIX) (XXX)

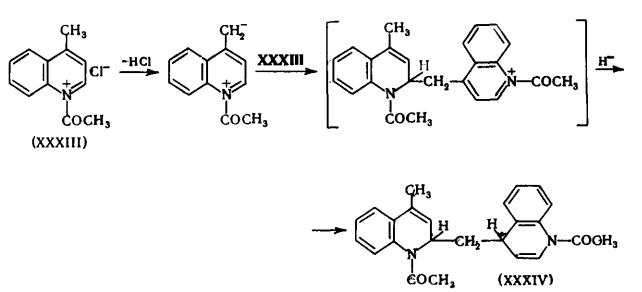
The hetarylation of indoles by *N*-acyl salts of six-membered nitrogen heterocycles [21,278,372,378-384] produces compounds of types



(XXXI) (XXXII)

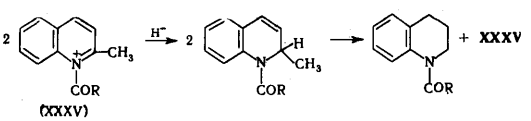
Thus 1-benzoyl-1,4-dihydro-4-indol-3'-ylpyridine has been obtained from pyridine, benzoyl chloride, and indole [178,378,380]. The yield is considerably lower when acetyl chloride is used, and with toluene-*p*-sulphonyl chloride the corresponding compound, formed in small quantities passed very readily into indolylpyridine. Under analogous conditions the reaction with *N*-acylacridinium salts gives only 3-acridin-9'-ylindoles [383,384]. The reaction of pyridine with indole in the presence of trichloroacetyl chloride involves the acylation (not the pyridylation) of indole, but in the presence of cyanogen bromide the pyridine ring is cleaved with formation of a pentadienal derivative of indole [379]. Isoindoles, in contrast to indoles, form 1,3-dipyridylisoindoles on interaction with pyridine and benzoyl chloride [385].

Many authors have pointed out that 1-acyl-2(and 4)-methylquinolinium salts cannot be used in hetarylations. Depending on the reaction conditions 1-acyl-4-methylquinolinium cations (XXXIII) are converted [386] either into 1-acyl-1,2-dihydro-4-methylquinolines or into "dimers" (at 50° and 100°C respectively). Detailed analysis of the mass spectrum of the "dimer" obtained with acetyl chloride indicates the structure (XXXIV). Its formation can be represented by the scheme (based on the dimerisation of 1-alkyl-4-methylquinolinium salts) [387]



(XXXIII) (XXXIV)

Formation of dimers has not been observed with 2-methylquinoline, probably because the methyl group is less strongly activated than in the 1-acyl-4-methylquinolinium ion [120]. 1-Acyl-1,2,3,4-tetrahydro-2-methylquinolines were always obtained when the reaction was conducted under various conditions, probably as a result of the disproportionation (with migration of hydrogen) of intermediate 1-acyl-1,2-dihydro-2-methylquinolines [380]:

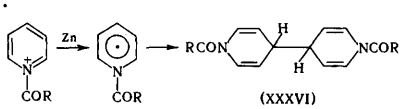


(XXXV)

5. One-electron Reduction of *N*-Acylated Heteroaromatic Cations

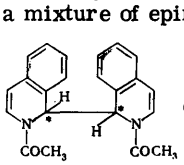
The strongly electrophilic character of *N*-acylated heteroaromatic cations is shown not only by their addition to reaction centres of high electron density or by their formation of charge-transfer complexes: reactions involving electron transfer and formation of the corresponding radicals are also facilitated in this series, since the one-electron reduction potentials of pyridinium cations fall when the electron-accepting properties of substituents attached to the heteroatom become stronger [388], and should be especially low with *N*-acylpyridinium salts and their benzologues. In fact, whereas *N*-alkylpyridinium salts are reduced only by sodium amalgam [389], zinc dust at room temperature or slightly above (30°C) is sufficient to reduce *N*-acylpyridinium salts; furthermore [74], a vigorous reaction with liberation of iodine is observed when potassium iodide is added to pyridine–arenesulphonyl chloride systems.

The formation of radicals by the action of benzoyl chloride and zinc dust on pyridine was first observed by Weitz et al. [390] Almost simultaneously Dimroth [391,392] observed the formation of a compound of type (XXXVI) in the reaction of acetic anhydride, pyridine, and zinc dust (more detailed information on its structure will be found in Ref. 393):



(XXXVI)

This reaction is characteristic of various *N*-acylpyridinium salts and their benzologues [394-400]. For example, isoquinoline forms a mixture of epimers of

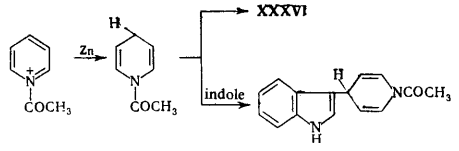


(XXXVII)

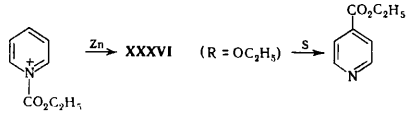
in equal proportions [397]. Acridine, however, does not yield a dimer but *N*-acetylacridan [401], which is probably explained by the greater stability of the *N*-acetylacridinyl radical: the latter does not recombine, but is reduced to the anion and then adds a proton.

For a long time the reaction could not be conducted with 2- and 4-methylpyridines [402,403], but the use of chloroformic esters as acylating agents enabled dimers of *N*-acylmethylpyridines and even of *N*-acyl-trimethylpyridine to be obtained [398-400]. With 4-substituted pyridines, however, 1,4-diacyl-1,4-dihydropyridine derivatives were isolated [399].

The *N*-acylpyridyl radicals formed in Dimroth's reaction are able not only to recombine but also to hetarylate nucleophilic aromatic or heteroaromatic compounds added to the reaction medium [28,404,405]:



4-Ethylpyridine has been prepared by the further reduction of pyridine with zinc in acetic acid (by Wibaut's method) [338,396,406-410], and the process has been exploited on an industrial scale [411-417]. The mechanism of the reaction has been discussed [338,408]. In spite of many unsuccessful attempts initially, it proved possible to obtain in this way 4-ethyl-2(and 3)-methylpyridines from 2- and 3-methylpyridines [418]. The use of chloroformic ester in this reaction yielded isonicotinic ester [419]:



---o0o---

Thus the chemistry of *N*-acylpyridinium salts and their benzo-analogues has already developed far enough to solve major theoretical and practical problems. From the point of view of synthetic organic chemistry several analogous compounds can be obtained by a different process, via the corresponding *N*-oxides. This line of attack, which has been especially broadly developed by Japanese chemists, is substantially different in its theoretical aspects, and therefore we have not dealt with it in the present paper.

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Karpov Physicochemical Institute,
Moscow

Donetsk State University

Lomonosov Moscow State University

U.D.C. 547.441; 547.307

Silicon-containing Isocyanates

V.P.Kozyukov, V.D.Sheludyakov, and V.F.Mironov

Methods of preparation, properties, and prospects for the application of silicon-containing isocyanates are surveyed. In the Review these compounds are divided into two classes—isocyanatosilanes and "*C*-functional" organosilicon isocyanates—because of the substantial differences in their properties and methods of preparation. Not only monomeric compounds but also oligomeric and polymeric products containing silicon and one or more isocyanato-groups are considered. The Review covers papers that appeared up to the end of 1971 and to some extent at the beginning of 1972. A list of 304 references is included.

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I. INTRODUCTION

The importance of organic isocyanates in theoretical and applied chemistry is well known, and progress in this field has been surveyed repeatedly [1-5]. The chemistry of organosilicon isocyanates began to be developed intensively only during the past decade, and their applied importance is continually increasing. Organosilicon isocyanates can be divided into two fundamentally different classes: the first comprises compounds containing the isocyanato-group directly attached to the silicon atom; and the second class includes isocyanato-alkyl, -aryl, -alkoxyl and other derivatives of silicon in which the isocyanato-group is separated from the silicon atom by some other group of atoms. Isolated data on the first type of compounds will be found in a review [6] on the pseudohalides of elements of Groups IIIb and IVb and in two papers [7,8]. However, most of the information on either type of silicon isocyanates has not been specially summarised. The present Review is an attempt to fill this gap.

II. COMPOUNDS CONTAINING AN ISOCYANATO-GROUP ATTACHED TO THE SILICON ATOM

1. Methods of Preparation

(*a*) Exchange between halogenosilanes and metal cyanates

A general method for the preparation of isocyanatosilanes is the double decomposition of halogenosilanes and metal cyanates [9-58]. This reaction has been used to prepare isocyanatosilanes of general formula $R_nSi(NCO)_{4-n}$, where $n = 1-3$ and R = Alk, Ar, OAlk, Hal, etc.

Although isocyanatosilanes are best obtained from bromosilanes, the more readily available chlorosilanes are often used. With iodosilanes yields are lower and the final products are less pure. Fluorosilanes do not undergo this reaction [27]. Replacement of the halogen by an isocyanato-group is effected by passing the vapour of the halogenosilane over the cyanate salt [29,30], in the melt [32], in an aprotic liquid organic solvent, or in the absence of a solvent [27,56].

The silver, mercury, lead, copper, tin, zinc, antimony, and thallium salts are generally employed for the double decompositions [27,33,34,43,44,47]. The use of freshly prepared salts taken in excess normally improves the yield [19,42,43,47]. The reaction of halogenosilanes with potassium and sodium cyanates is considerably more difficult. For example, silicon tetraiodide has not reacted with potassium cyanate at 20°C after twelve days [30], and the prolonged heating of silicon tetrachloride with potassium and sodium cyanates gives a low yield of silicon tetraisocyanate [9,45]. Satisfactory yields of this product are obtained when silicon tetrachloride vapour is passed over the finely ground or molten salts of alkali or alkaline-earth metals at temperatures above 200°C. [45] Trimethylsilyl isocyanate has been obtained under similar conditions [34,57].

Isocyanatosilanes have recently been obtained in high yields by the reactions of chlorosilanes with potassium and sodium cyanates in liquid sulphur dioxide [35], and also with the lithium salt in benzene [36]. The most complete series of compounds $R_nSi(NCO)_{4-n}$ have been obtained with R = Alk and C_6H_5. [12,18,19] Isocyanatosilanes having a vinyl, phthalocyanine, alkoxyl, aroxyl, or organosilyl group attached to the silicon atom are obtained by the same scheme as are alkyl and aryl derivatives [14,18,31,35,37,38,41,49].

In the preparation of silicon tetraisocyanate from the tetrachloride and silver cyanate the reaction takes place step by step and is accompanied by partial hydrolysis of the reaction products [10,17]. In this way the compounds

$$Cl_3SiNCO,\quad Cl_2Si(NCO)_2,$$

$$Si(NCO)_4;\ (OCN)_3SiOSi(NCO)_3 \text{ and } (OCN)_3SiOSi(NCO)_2OSi(NCO)_3$$

were isolated.

Partly halogenated silanes are also used for the preparation of isocyanatosilanes [13,59]: e.g.

$$2SiHCl_3 + 8AgOCN \rightarrow 2Si(NCO)_4 + 6AgCl + 2Ag + H_2$$

Finally, it is noteworthy that isothiocyanato- and mercapto-groups can also be replaced by the isocyanato-group [11,27]:

$$Cl_3SiSH + 4AgNCO \rightarrow Si(NCO)_4 + AgSH + 3\,AgCl$$

$$Me_2Si(NCS)_2 + 2AgNCO \rightarrow Me_2Si(NCO)_2 + 2AgSCN$$

(*b*) Aspects of exchange reactions

Eaborn arranged organosilicon compounds in what he termed "conversion series", characterising their capacity for irreversible transformation on reaction with metal

salts. With the triethylsilyl derivatives, for example, the series is (R = C_2H_5) [26,27,60]

$$R_3SiI \xrightarrow{Ag_2S} (R_3Si)_2S \xrightarrow{AgBr} R_3SiBr \xrightarrow{NaH} R_3SiH \xrightarrow{AgCN} R_3SiNC \rightarrow$$
$$\xrightarrow{AgCl} R_3SiCl \xrightarrow{AgSCN} R_3SiNCS \xrightarrow{AgNCO} R_3SiNCO \xrightarrow{KOAc} R_3SiOC(O)Me \rightarrow$$
$$\xrightarrow{H_2O} (R_3Si)_2O \xrightarrow{\text{heavy-metal fluorides}} R_3SiF$$

Hence it follows that isocyanatosilanes cannot be obtained from acyloxysilanes, siloxanes, and fluorosilanes. Analogous conversion series have been established for methylsilanes $(CH_3)_3SiX$, dialkyl(and aryl)silanes R_2SiX_2 [23,27], and salts of other metals—mercury, tin, antimony, cadmium, zinc, and copper.

Under the conditions of a heterolytic reaction mechanism the factor determining the sequence of compounds in conversion series is probably the affinity of the various functional groups for the silicon atom, although other factors are also important. This conclusion is supported by the coincidence of the conversion series with the sequence of compounds in order of increasing energy of the ionic Si–X bonds (X = I, S, Br, etc.) [27].

On the other hand, Anderson showed [24,60-66] that silicon; germanium, and phosphorus isocyanates undergo exchange reactions with compounds of elements in the middle of the Periodic System provided that the most volatile component is removed from the reaction mixture. Such sequences of conversion of some compounds into others were termed "volatility series". Examples of such reactions are

$$Me_2Si(NHPh)_2 + Ph_2Si(NCO)_2 \rightarrow Me_2Si(NCO)_2 + Ph_2Si(NHPh)_2$$
$$Et_3GeOSO_2R + Ph_3SiNCO \rightarrow Et_3GeNCO + Ph_3SiOSO_2R$$

In the triethylsilyl series the conversions

$$Et_3SiNHPh \rightarrow Et_3SiNCS \rightarrow Et_3SiI \rightarrow Et_3SiNCO \rightarrow Et_3SiBr \rightarrow Et_3SiCl$$

are possible. It must be noted that the sequences of exchange reactions in "conversion series" and "volatility series" often do not coincide.

(*c*) Reactions of organosilicon compounds with isocyanic acid

The original attempts to use isocyanic acid to replace chlorine atoms in chlorosilanes by the isocyanato-group were unsuccessful, in spite of the use of aluminium, zinc, iron, and mercury chlorides as catalysts [11,34]. It was found, however, that isocyanatosilanes are easily formed if the hydrogen chloride liberated is bound by tertiary amines or by amides of carboxylic acids [37,67,68]:

$$R_nSiCl_{4-n} + (4-n)\,HNCO + (4-n)\,R'_3N \rightarrow R_nSi(NCO)_{4-n} + (4-n)\,R'_3N \cdot HCl$$

The reaction must be conducted in the presence of a slight excess of chlorosilanes, which stabilise isocyanic acid and isocyanatosilanes [68]. Alkoxy- and aryloxy-isocyanatosilanes have been obtained by this method [69]. According to patent claims [70] silanols, e.g. triphenylsilanol, can be used as initial compounds in the reaction with isocyanic acid. In view of the ready availability of isocyanic acid, obtained by the pyrolysis of cyanuric acid or urea, its use for the preparation of isocyanatosilanes is extremely promising.

(*d*) Disproportionation

Many observations have been made of the formation of isocyanatosilanes by disproportionation [10,71-79]:

$$Si(NCO)_4 + Si(NCS)_4 \rightarrow SCNSi(NCO)_3$$
$$Si(NCO)_4 + SiCl_4 \rightarrow Cl_3SiNCO + Cl_2Si(NCO)_2 + ClSi(NCO)_3$$
$$Si(NCO)_4 + SbF_3 \rightarrow F_3SiNCO + F_2Si(NCO)_2 + FSi(NCO)_3$$

However, isolation of the reaction products is extremely difficult owing to their tendency to symmetrisation. This applies especially to compounds of the type $XSi(NCO)_3$ (where X = Cl, OCH_3, F) [10]. Compounds of types $(CH_3)_nSi(NCO)_{4-n}$ and $(CH_3)_nSiCl_{4-n}$ ($n \geq 1$) exhibit a tendency to disproportionate only about one-thousandth of that shown by silicon tetraisocyanate and the tetrachloride or tetrabromide [10,72-74].

A quantitative study by means of proton magnetic resonance spectroscopy of the exchange of isocyano, isocyanato, and isothiocyanato for chloro, bromo, alkoxyl, alkylthio, etc. in mono- and di-methylsilanes [75-77] showed that, with rare exceptions [75], the position of equilibrium conforms to a random distribution. Equilibrium constants have been determined for several exchange reactions [75-77,80].

Disproportionation has found application only in the preparation of fluoroisocyanatosilanes.

(*e*) Other methods of preparation of isocyanatosilanes

Besides the above general methods there are several specific reactions one of whose products is a compound containing an Si–NCO fragment. Gilman et al. [46] obtained triphenylsilyl isocyanate by the reactions

$$Ph_3SiCl + \begin{matrix} Na \\ \diagdown \\ NCOOEt \\ \diagup \\ H \end{matrix} \rightarrow Ph_3SiNCO + EtOH + NaCl$$
$$Ph_3SiCl + NH_2CONH_2 \xrightarrow{Cu} Ph_3SiNCO + NH_4Cl$$

Goubeau and Paulin [34] prepared trimethylsilyl isocyanate and dimethylsilylene di-isocyanate by the reaction of urea at 240–320°C with trimethylchlorosilane and dimethyldichlorosilane respectively, the yield in the latter case being 5–10%.

Pump and Rochow [81] showed that trimethylsilyl isocyanate is formed in the thermal decomposition of silicon derivatives of carbamic acid:

$$ROC(O)Cl + NaN(SiMe_3)_2 \rightarrow RO-\overset{\overset{N-SiMe_3}{\|}}{C}-OSiMe_3 \rightarrow Me_3SiNCO + Me_3SiOR$$

The reaction of carbon dioxide with bistrimethylsilylsodamide obviously has a similar mechanism, via trimethylsilyl isocyanate as an intermediate product [82]. The formation of this isocyanate has been observed also in the reaction of carbonyl chloride with hexamethyldisilazane [83-85] and in the interaction of technical calcium or barium cyanamide with trimethylchlorosilane in a lithium chloride–sodium chloride melt at 400°C [86].

Zhinkin and his coworkers [87-92] suggested an interesting route for the preparation of isocyanatosilanes:

$$(Me_3Si)_2NH + PhNCO \rightarrow PhNHC(O)N(Ph)SiMe_3 + Me_3SiNCO$$
$$Me_3SiNHC(O)N(Ph)SiMe_3 \xrightarrow{120°C} Me_3SiNCO + Me_3SiNHPh$$

Unsymmetrical organodisilazanes yield two isocyanatosilanes and two aminosilanes in this reaction [92]. Mono-, di-, and tri-isocyanatomethylsilanes, as well as isocyanatosilanes containing unsubstituted hydrogen, have been obtained by the pyrolysis of *N*-silylated ureas [94-96]:

$$Me_nSi(NHCONPh_2)_{4-n} \rightarrow Me_nSi(NCO)_{4-n} + (4-n)\,Ph_2NH$$

$$NH_2CONH_2 + (HSiMe_2)_2NH \rightarrow HSiMe_2NCO + NH_3$$

$$NH_2CONH_2 + (Me_3Si)_2NH \rightarrow Me_3SiNCO + NH_3$$

$$(PhNH)_2CO + (Me_3Si)_2NH \rightarrow Me_3SiNCO + Ph_2NH$$

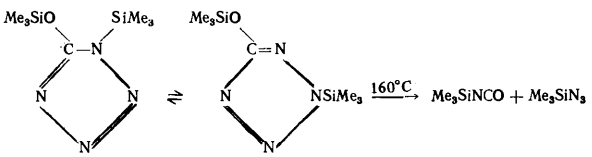
Silyl isothiocyanates are readily formed by the action of sulphur on silicon isocyanides [97,98]. Nevertheless, mild oxidation of the latter with mercury(II) oxide or silver(I) oxide does not yield isocyanatosilanes but products in which the silicon–nitrogen bond has been ruptured [7,56,98]. Strong oxidants (lead dioxide, manganese dioxide, and sodium peroxide) react with trialkylsilyl isocyanides only on heating, but formation of isocyanatosilanes has not been reported at all [52,99,100].

Heating trimethylsilyl isoselenocyanate in dry air gives selenium, trimethylsilyl isocyanate, and trimethylsilyl cyanide [52].

A peculiar type of exchange occurs in the reaction between chlorosilanes and chlorine isocyanate [95]:

$$R_3SiCl + ClNCO \rightarrow R_3SiNCO + Cl_2$$

Finally, trimethylsilyl isocyanate has been obtained by the pyrolysis of a mixture of tautomeric forms of 1-hydroxy-*NO*-bistrimethylsilyltetrazole [101]:



2. Structure and Properties of Isocyanatosilanes

(*a*) Physical properties

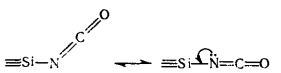
Pseudohalide groups are polyatomic, linear, electronegative, and able to develop a negative inductive effect along a bond with a metal. All these properties are exhibited by isocyanato-groups in silanes. Nevertheless, in contrast to organic isocyanates, the proximity of the isocyanato-group to a silicon atom having vacant *d*-orbitals may produce special structural features connected with the ability of the isocyanato-group to be conjugated by means of its π-system or its donor atoms (nitrogen or oxygen). These peculiarities may be represented by the structural isomerism

$$\underset{\text{isocyanate form}}{Si{-}N{=}C{=}O} \rightleftharpoons \underset{\text{siloxynitrile form}}{Si{-}O{-}C{\equiv}N}$$

and by the partly double-bond character of the silicon–nitrogen bond, as a consequence of which the Si–N=C=O unit should be spatially linear.

The isocyanate form is generally accepted, although problems of the three-dimensional structure of the molecules, and in particular linearity of the Si.N : C : O system, have still been inadequately studied. Preference has been given to the iso-structure on the basis of molecular refractions, infrared, Raman, nuclear magnetic resonance, and mass spectra, and also the observed analogy in properties between isocyanatosilanes and the thermodynamically more stable (relative to the isomeric cyanic esters) organic isocyanic esters.

Spectral data for trimethylsilyl isocyanate [99], compounds $(C_6H_5O)_nSi(NCO)_{4-n}$ (n = 1–3) [103,104], trichlorosilyl isocyanate [104], and several other isocyanates and isothiocyanatosilanes [37,49,105-115] confirm their iso-structure. The infrared spectra of isocyanatosilanes contain bands corresponding to the characteristic stretching vibrations ν_{sym}^{NCO} = 1475–1325, ν_{asym}^{NCO} = 2290–2190, and δ_{Si-NCO} = 616, 606 cm^{-1}. [37,99,102-105,116-118] Vibrations of the Si–NCO bond are probably responsible also for bands around 2381 and 1972–2000 cm^{-1} [117,118]. In the series of compounds $(CH_3)_nSi(NCO)_{4-n}$, moreover, the ν_{sym}^{NCO} frequency increases with n; the intensity and the width of the infrared bands remain typical of organic isocyanates [99,116,119-121]. The probable reason is $p \rightarrow d$ interaction between silicon and nitrogen atoms, which governs the multiplicity of the Si–NCO bond and the appearance of the resonance structures [116]



The infrared and Raman spectra of silyl isocyanate [122], trichlorosilyl isocyanate, and chlorosilylidyne tri-isocyanate are consistent with this hypothesis, and agree well with the formal charge distribution in silyl isocyanate and the octet rule [123].

The carbon-13 nuclear magnetic resonance spectra show that all the carbon atoms in silicon tetraisocyanate are of the same type [119]. According to the proton magnetic resonance spectra protons of only one type are present in silyl isocyanate and isothiocyanate and in disilylcarbodiimide [48]. The infrared and Raman spectra of the tetraisocyanate in the range 4000–80 cm^{-1} are very simple, which indicates that the molecule is highly symmetrical, and corresponds to a tetrahedral model [116,119,120].

Electron diffraction examination of silyl isocyanate [124], trimethylsilyl isocyanate [125], silicon tetraisocyanate [126], chlorosilylidyne tri-isocyanate, dichlorosilylene di-isocyanate, trichlorosilyl isocyanate [127], and trifluorosilyl isocyanate [128] shows that the Si–N–C angles are smaller than 180°, being respectively 151.7 ± 1.2°, 154 ± 2° (150 ± 3°), 146.4°, 145.0°, 136.0°, 138.0°, and 160.7 ± 1.2°. The results no longer correspond to a rigid model (of symmetry D_{2d}) but to a model with free rotation about the silicon–nitrogen bond (symmetry C_{3v} [125]), and indicate the absence of appreciable double-bond character. In the Reviewers' opinion, however, a final conclusion on this matter is premature.

Mass-spectroscopic investigation of the tetraisocyanate reveals the formation of a molecular ion $Si(NCO)_4^+$. [129]

Isocyanatosilanes, other than the gaseous silyl and trifluorosilyl isocyanates, are colourless liquids or solids with an acrid smell. The odour of triethylsilyl isocyanate recalls that of camphor [12].

The boiling points of compounds R_3SiX vary with the nature of X in the sequence [61] Cl < Br = NCO < I < NCS < < NHC_6H_5.

Several alkyl- and aryl-isocyanatosilanes exhibit a tendency to supercooling [11]. Members of the series $(CH_3)_nSi(NCO)_{4-n}$ (n = 1–3), on the other hand, have sharp melting points. Isocyanatosilanes burn readily in air, dissolve well in organic solvents [17,71], and are mostly thermostable compounds [16]. Their stability is greater the lower the electronegativity of other substituents attached to the silicon atom [130], and is sharply diminished by contamination with silver cyanate, cyanic acid, diborane, or triethyl phosphine [29].

The values of the Trouton constant suggest that there is little or no association of isocyanatosilanes in the liquid state [18,19,29].

(v) Chemical properties

The pseudohalide character of the NCO group in isocyanatosilanes is shown in their ability to react with proton-containing compounds, either with replacement of the isocyanato-group [6]

$$R_3SiNCO + H{-}X \rightarrow R_3SiX + HNCO$$

or with addition of the elements of H–X at the double bond in the isocyanato-group

$$R_3SiNCO + H{-}X \rightarrow R_3SiNHC(O)X$$

Hydrolysis. All isocyanatosilanes, on treatment with water, are hydrolysed to silanols and isocyanic acid. Qualitative observations show that the rates and the heats of hydrolysis of the compounds $Alk_nSi(NCO)_{4-n}$ fall with increase in n [12,19]. The stability of triphenylsilyl and triethylsilyl isocyanates towards water is due to their poor solubility, since they are rapidly hydrolysed on the addition of alcohol, acetone, or dioxan [12,20,27,46]. The isocyanatosilanes $Cl_nSi(NCO)_{4-n}$, $F_nSi(NCO)_{4-n}$, and $(OCN)_3Si.O.Si(NCO)_3$ undergo vigorous hydrolysis with the evolution of heat [12,71,73]. Silicon tetraisocyanate forms products of partial hydrolysis when insufficient water is used [17]. Methoxy- and phenoxy-isocyanatosilanes hydrolyse at a moderate rate. The ease of hydrolysis of isocyanatosilanes in comparison with silicon pseudohalides of the same type places them in the sequence—$R_3SiNCO < R_3SiNCS < R_3SiNC$ [27].

The reaction of isocyanatosilanes with water is used for the quantitative determination of the isocyanato-group [12,16,27,71]. However, more reliable results are obtained by the Dumas determination of nitrogen [12,17–19].

Reactions with alcohols. A detailed study of the alcoholysis of isocyanatosilanes was made in work [34] which confirmed earlier results obtained by Forbes and Anderson [11,18,71] on the formation of alkoxysilanes and the corresponding urethanes. This showed that increase in the size and in the degree of branching of the radical, either in the silane or in the alcohol, leads to a fall in the rate of alcoholysis [34,46]. The two schemes

$$R_3SiNCO + R'OH \begin{cases} \xrightarrow{1} R_3SiOR' + HNCO \xrightarrow{R'OH} H_2NC(O)OR' \\ \xrightarrow{2} R_3SiNHC(O)OR' \xrightarrow{R'OH} R_3SiOR' + H_2NC(O)OR' \end{cases}$$

were suggested [34] to explain the course of the reaction. In the first stage of interaction with an aqueous alcohol, isocyanic acid is formed, and can be titrated [12]. Nevertheless, its presence was not detected in the reaction with an anhydrous alcohol [34].

Considerable doubt must attach to the reported [131] preparation of urethanes containing a silicon–nitrogen bond by heating dibutylsilylene di-isocyanate with higher alcohols and glycols, in view of the lack of adequate characterisation of the products. This applies equally to the synthesis of a polyurethane based on diphenylsilanediol and dimethylsilylene di-isocyanate [132], since, in contrast to alcohols, silanols and silanediols are inert towards e.g. trimethylsilyl isocyanate [133]. The claimed formation [134] of polysilylurethanes containing $\gtrless$Si.NH.CO.OR'– by the reaction of $R_nSi(NCO)_{4-n}$ and $(RO)_nSi(NCO)_{4-n}$ ($n = 0–2$) with glycols $R'(OH)_2$ and a polyethylene glycol ether is just as improbable.

Reactions with amines. In early studies of the reaction of isocyanatosilanes with amines it was erroneously concluded that the isocyanato-group was eliminated [62,135,136]. By the use of ammonia and primary and secondary aliphatic and aromatic amines with a variety of isocyanatosilanes Goubeau and Heubach as well as other workers were able to show [38,65,84,133] that the amines add at the C=N bond to form N-silylureas:

$$Me_nSi(NCO)_{4-n} + R_mNH_{3-m} \rightarrow Me_nSi(NHCONH_{2-m}R_m)_{4-n}$$

The reactivity of amines towards silicon isocyanates fell in precisely the same sequence as their reactivity towards organic isocyanates [43]:

$$AlkNH_2 > Alk_2NH > ArNH_2 \gg ArNHR > Ar_2NH$$

Silicon tetraisocyanate was found to be more reactive than its alkyl and aryl derivatives [62,133]: with trimethylsilyl isocyanate, for example, addition was observed only with amines of basicity $pK > 10$ [137]. The steric factor plays an important part, besides the basicity of the amine: 2,6-dibromoaniline reacts slowly even with silicon tetraisocyanate [43].

Symmetrical di-isocyanatodisilanes form disilylureas in conformity with the general scheme [38]. Tertiary amines do not react with isocyanatosilanes [133]. Hydrazines and silylhydrazines give silylsemicarbazides with trimethylsilyl isocyanate; the isocyanatosilane acts more selectively in these reactions than do organic isocyanates [137]. Free hydrazine undergoes exchange with trimethylsilyl isocyanate, and adds at the isocyanato-group [84,137].

Other reactions. The isocyanato-group in triethylsilyl isocyanate does not react with methylmagnesium iodide, nor do those in the tetraisocyanate interact with dimethylmercury [19]. Triphenylsilyl isocyanate adds phenyl-lithium and phenylmagnesium bromide with difficulty at the carbonyl bond to form after hydrolysis triphenylsilanol and benzamide [46]. With bistrimethylsilylsodamide isocyanatosilanes are converted into disilylcarbodi-imides [138–141].

In the reaction of oxirans with isocyanatosilanes $R_nSi(NCO)_{4-n}$ ($n = 0–3$) the ring is opened [142–144]:

$$R_nSi(NCO)_{4-n} + CH_2{-}CH_2 \overset{O}{\diagup\diagdown} \xrightarrow[R_3N]{P \geq 1\ atm} R_n(OCN)_m Si(OCH_2CH_2NCO)_{4-m-n}$$

Use in the reaction of aldehydes [145] or of ketones containing an α-hydrogen atom [146] gives polymeric products of undetermined structure.

Sulphur tetrafluoride [147] and carbonyl fluoride [148] rupture the silicon–nitrogen bond in isocyanatosilanes:

$$Si(NCO)_4 + 4SF_4 \rightarrow SiF_4 + 4F_2S{=}N{-}C(O)F$$
$$Me_nSi(NCO)_{4-n} + (4-n)COF_2 \rightarrow (4-n)Me_nSiF_{4-n} + (4-n)FC(O)NCO$$

The reactions of isocyanatosilanes containing unsubstituted hydrogen are illustrated by the examples [29]

$$H_3SiNCO + NaOH \rightarrow NaOCN + H_2 + SiO_2$$
$$H_3SiNCO + H_2CO_3 \rightarrow H_2 + SiO_2 + CO_2 + HNCO$$
$$H_3SiNCO + MeOH \rightarrow SiH_4 + (MeO)_3SiH + (MeO)_4Si + MeOC(O)NH_2$$
$$H_3SiNCO + HCl \rightarrow H_3SiCl + {}^1/_3(HNCO)_3$$
$$H_3SiNCO + BF_3 \rightarrow H_3SiF + F_3BNCO \rightarrow BF_3 + [B(NCO)_3]_n$$

In this case addition products are not formed with diborane either at 20° or at –78°C, although the isocyanates are

decomposed in the presence of diborane at room temperature.

In conclusion, tri-isocyanatosilanes $XSi(NCO)_3$ (X = Cl, F, CH_3O, etc.) exhibit a strong tendency to disproportionate, which is greatly hindered by isolation of the compounds in pure form [10].

Isocyanatosilanes containing unsubstituted hydrogen can take part in hydrosilylation in conformity with the generally accepted scheme. They undergo neither di-, tri-, and poly-merisation nor decarboxylation when boiled for a long time with such catalysts as metal carbonyls, dimethyl tolyl phosphate, methylphosphafluorene oxide, and bis-*P*-methyl-*P*-phenyl-thiophosphoryl [94].

3. Prospects for the Application of Isocyanatosilanes

The great reactivity of isocyanatosilanes enables them to be used in the manufacture of various polymeric materials. Thus they have been proposed for the production of plastics [45], insulating materials, dielectrics [79], and pesticides [70,79], and as textile finishes [149], hydraulic fluids, components of self-setting compositions [150,151], and catalysts in the synthesis of polyurethanes, for the water-repellent treatment of glass, porcelain, and cloth, and for other purposes [33,44,57,68]. Polymers obtained by the reaction of dialkylsilylene di-isocyanates with amines or alcohols [134,142-144], aldehydes [145], and ketones [146] are suitable for the production of moulded articles and glass—plastic laminates, as additives to rigid foam plastics, and as adhesives for wood, metals, and other materials. Products of the interaction of silanediols† with isocyanatosilanes have been recommended for coating the internal surfaces of fuel tanks [132].

Compounds of type $(OCN)_nSi(OCH_2CH_2NCO)_{4-n}$ are capable of spontaneous polymerisation with the formation of resins or flexible films possessing good adhesion to glass [142-144]. Several materials based on isocyanatosilanes exhibit short-term fire-resistance and high thermal stability [68]. Modification with isocyanatosilanes sharply increases the adhesion of silicone rubbers to copper or brass [152]. Fillers treated with isocyanatosilanes improve the stability of polyurethane coatings for wood, metals, glass, concrete, and other materials [153].

A second promising usage of isocyanatosilanes is as ancillaries in organic synthesis. For example, the quantitative formation of silylureas by the reaction of isocyanatosilanes with amines and the ready hydrolysis of the products have been used to develop a general method for the preparation of ureas [43] which dispenses with the difficultly available alkyl isocyanates and alkyl(aryl, dialkyl, diaryl)carbamoyl chlorides.

III. "C-FUNCTIONAL" ORGANOSILICON ISOCYANATES

1. Methods of Preparation

(*a*) From derivatives of carboxylic acids

In contrast to isocyanatosilanes, carbofunctional organosilicon isocyanates (primarily compounds having isocyanato-alkyl and -aryl groups attached to the silicon atom) were little studied until quite recently. The first such compound was obtained in 1959 from *p*-trimethylsilylbenzoyl azide [154]:

$$p\text{-}Me_3SiC_6H_4COCl \xrightarrow{NaN_3} p\text{-}Me_3SiC_6H_4CON_3 \xrightarrow[-N_2]{t^\circ} p\text{-}Me_3SiC_6H_4NCO$$

Intermediate formation of isocyanates has been observed also in the decomposition of azides of silylated aliphatic acids [93,94].

The intermediate formation of 3-ethyldimethylsilylpropyl isocyanate has been noted during oxidation of the corresponding amide by lead tetra-acetate [93,94]:

$$RC(O)NH_2 \xrightarrow[HCON(CH_3)_2]{Pb(OAc)_4} [R{-}N{=}C{=}O] \xrightarrow{C_5H_5NH_2} RNHC(O)NHC_5H_5,$$

(R = Et—Si(Me)(Me)—$(CH_2)_3$—)

(*b*) Hydrosilylation of alkenyl isocyanates

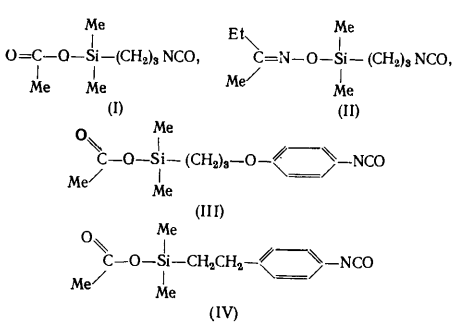
A convenient route for the preparation of monomeric, oligomeric, and polymeric organosilicon *C*-isocyanates consists in the catalytic addition of silanes containing unsubstituted hydrogen to unsaturated organic isocyanates. Monomers containing one, two, or three hydrolysable groups attached to the silicon atom can be obtained by this reaction [94,155-163].

Replacement of the chlorine atoms in trichlorosilane by alkyl groups leads to an appreciable decrease in the rate of addition to allyl isocyanate [94,156]:

$$MeCl_2SiH + CH_2{=}CHCH_2NCO \xrightarrow[3\ h]{H_2PtCl_6} Me{-}Si(Cl)(Cl)(CH_2)_3NCO \quad (80\%)$$

$$Me_2ClSiH + CH_2{=}CHCH_2NCO \xrightarrow[40\ h]{H_2PtCl_6} Cl{-}Si(Me)(Me)(CH_2)_3NCO \quad (40\%)$$

This reaction does not take place with methyldiethylsilane and triethylsilane. Several isocyanates, e.g. of the types



have been obtained by the addition of incompletely substituted silanes containing acyloxy- or hydroxyamino-groups to allyl, *p*-allyloxyphenyl, or *p*-vinylphenyl isocyanate in the presence of catalytic quantities of an ethylene–platinum complex [157]. Silicon-containing urethano-isocyanates have been prepared by the action of siloxanes and incompletely substituted silanes on urethano-isocyanates (products of the interaction of allyl and methylallyl alcohols with tolylene di-isocyanate) [158,159].

In contrast to silyl acetates, tetramethyldisiloxane does not add to allyl isocyanate [94,155]. However, a di-isocyanate could be obtained from another partly substituted silane, *p*-bisdimethylsilylbenzene [94,155], where addition takes place in steps.

†The products formed with alcohols and silanediols obviously do not possess a polysilylurethane structure (Subsection 2*b*), but comprise a mixture of polyoxasilaalkylenes or polysiloxanes with organic urethanes and polymeric forms of isocyanic acid.

The catalysts used have included, not only hexachloroplatinic acid and the ethylene–platinum complex, but also other platinum derivatives, palladium compounds, and certain catalysts of ionic and free-radical reactions [96,156–162].

In contrast to allyl isocyanate, isopropenyl isocyanate exhibits surprising inertness towards not only trialkylsilanes and tetramethyldisiloxane but also partly substituted alkoxy- and chloro-silanes [94].

The isocyanato-group, like the isoelectronic keten grouping [164,165], remains unchanged during hydrosilylation. Moreover, incompletely substituted silanes (especially those containing silicon–chlorine bonds) have a stabilising effect on the initial and the final isocyanates, diminishing their tendency to polymerise when heated.

Examination of the addition products of incompletely substituted silanes to allyl isocyanate by means of proton magnetic resonance spectroscopy has shown [94] that they all contain the isocyanato-group in the γ-position relative to the silicon atom.

(*c*) Reaction of silylated amines with carbonyl chloride

Another convenient method for obtaining organosilicon *C*-isocyanates is the action of carbonyl chloride on the corresponding primary amines. Aliphatic isocyanates were first obtained in this way [93,163,166]:

$$2R_3Si(CH_2)_nNH_2 + COCl_2 \xrightarrow{20^\circ C} R_3Si(CH_2)_nNHCOCl + R_3Si(CH_2)_nNH_2 \cdot HCl$$
$$R_3Si(CH_2)_nNHCOCl \xrightarrow{110-150^\circ C} R_3Si(CH_2)_nNCO + HCl$$
$$R_3Si(CH_2)_nNH_2 \cdot HCl + COCl_2 \xrightarrow{110-150^\circ C} R_3Si(CH_2)_nNCO + 3HCl$$
$$2R_3Si(CH_2)_nNH_2 + 2COCl_2 \rightarrow 2R_3Si(CH_2)_nNCO + 4HCl$$
(R=Alk, Ar; $n = 1; 3$)

Dimeric compounds having a dioxouretidine structure are formed by a side-reaction [166]. 3-Trimethylsilylpropyl isocyanate isolated in pure form was completely stable, and did not dimerise either on storage or when distilled.

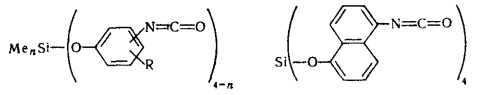
With amines containing alkoxy- or siloxy-groups attached to silicon, carbonyl chloride may act also on the silicon–oxygen bonds [94,163,167–169]:

$$(EtO)_3Si(CH_2)_3NH_2 \xrightarrow[110-120^\circ C]{COCl_2} Cl_n(EtO)_{3-n}Si(CH_2)_3NCO + EtOC(O)Cl + HCl$$

$$NH_2(CH_2)_3\underset{\underset{Me\ Me}{|\ \ |}}{SiOSi}(CH_2)_3NH_2 \xrightarrow[-4HCl]{COCl_2} 2Cl\underset{\underset{Me}{|}}{Si}(CH_3)_3NCO + CO_2$$

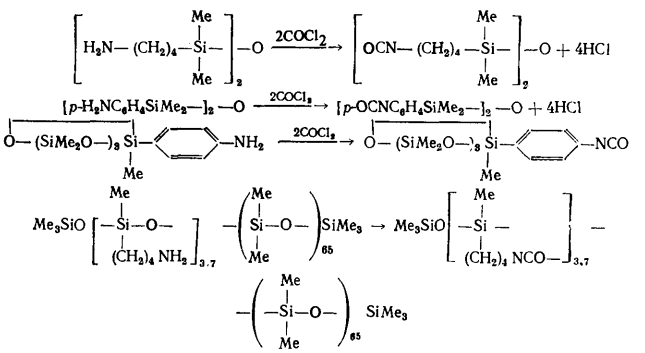
$$NH_2(CH_2)_4\underset{\underset{Me\ Me}{|\ \ |}}{SiOSi}(CH_2)_4NH_2 \xrightarrow{COCl_2} Cl\underset{\underset{Me}{|}}{Si}(CH_2)_4NCO + OCN(CH_2)_4\underset{\underset{Me\ Me}{|\ \ |}}{SiOSi}(CH_2)_4NCO$$

Silyl ethers of amino-alcohols of type $R_2Si(OCH_2CH_2NH_2)_2$ are completely cleaved at the silicon–oxygen bond on reaction with carbonyl chloride, but the final products were not identified [168]. Nevertheless, the analogous aminophenol and aminonaphthol derivatives, whether as the free bases or as the hydrochlorides, form the corresponding isocyanates [168,170]:



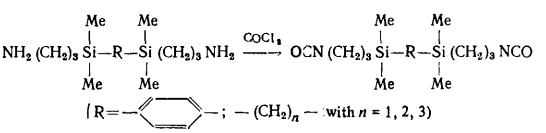
($n = 1-3$; R = H, Me)

Organic mono- and di-isocyanates containing silicon have been obtained by treating aminoalkyl and aminoaryl derivatives of di-, tetra-, and oligo-siloxanes with carbonyl chloride in toluene [169]:



A striking feature of this work is that the siloxane bonds remain unchanged under the severe conditions of treatment with carbonyl chloride and hydrogen chloride.

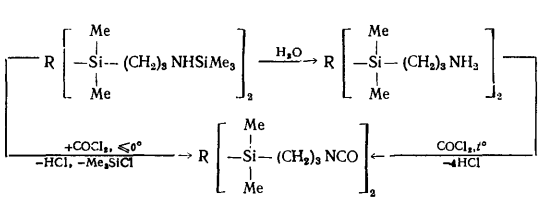
A new type of difunctional organosilicon monomers was obtained by the action of carbonyl chloride on diamines containing alkylene or phenylene bridges between the silicon atoms [94,171]:



Whether in a diamine with an arylene bridge or in 3-phenyldimethylsilylpropylamine the Si–Ar bond is stable towards the chlorinating action of carbonyl chloride, hydrogen chloride, and the chloroformamido-group [94,171].

(*d*) Action of carbonyl chloride on *N*-silylamines

It was discovered in 1969 that organosilicon di-isocyanates of the above type can be obtained in high yields and under milder conditions by the action of carbonyl chloride on the *N*-trimethylsilyl derivatives of the amines [94,172–176]:



Monoisocyanates have been obtained similarly [94,174–176]:

$$MeEt_2SiH + CH_2{=}CHCH_2NHSiMe_3 \rightarrow MeEt_2Si(CH_2)_3NHSiMe_3$$
$$MeEt_2Si(CH_2)_3NHSiMe_3 \xrightarrow[\leqslant 0^\circ]{COCl_2} MeEt_2Si(CH_2)_3NCO + Me_3SiCl$$

These observations provided an extraordinarily simple method for preparing 3-dimethylchlorosilylpropyl isocyanate [173,177]:

$$Me_2SiHCl + CH_2{=}CHCH_2NH_2 \rightarrow CH_2{=}CHCH_2NHSiMe_2H \xrightarrow{H_2PtCl_6} \rightarrow \left[-CH_2CH_2CH_2NH\underset{\underset{Me}{|}}{Si}-\right]_x \xrightarrow[-xHCl]{xCOCl_2} xClMe_2Si(CH_2)_3NCO$$

It was subsequently established[173-176] that the reaction of carbonyl chloride with *N*-silylated primary amines is general in character, and can be used to obtain not only organosilicon but any other isocyanates containing groups sensitive to heating and to the action of hydrogen chloride, carbonyl chloride, and the chloroformamido-grouping. For example, saturating the reaction mass with carbonyl chloride at a low temperature removes hydrogen chloride rapidly, which has enabled the previously difficultly accessible disiloxane di-isocyanates to be obtained:

$$[Me_3SiNH(CH_2)_3-SiMe_2-]_2-O \xrightarrow[-2HCl]{2COCl_2} OCN(CH_2)_3-\underset{\underset{Me}{|}}{\overset{\overset{Me}{|}}{SiO}}-\underset{\underset{Me}{|}}{\overset{\overset{Me}{|}}{Si}}-(CH_2)_3NCO + 2Me_3SiCl$$

N-Silylated amines react with carbonyl chloride under very mild conditions (−60° to 0°C). The yields of isocyanates reach 90–99%.

The pattern observed might have been quite different if the reaction had involved initial cleavage of the silicon–nitrogen bond in the silylamine. In fact the intermediate carbamoyl chlorides are quite stable under the reaction conditions, and decompose into hydrogen chloride and the isocyanate only when heated to ~100°C and above:

$$R-\underset{\underset{H}{|}}{N}-SiMe_3 \xrightarrow[-Me_3SiCl]{COCl_2} R-\underset{\underset{H}{|}}{N}-\underset{\underset{Cl}{|}}{C}=O \underset{\leftarrow}{\overset{\sim 100^\circ}{\rightarrow}} RNCO + HCl$$

To explain the formation of hydrogen chloride with such a reaction scheme it was necessary to assume that trimethylsilyl chloride already reacts with the carbamoyl chloride under the mild conditions, yielding ultimately the isocyanate:

$$R-\underset{\underset{H}{|}}{N}-\overset{\overset{O}{\|}}{C}-Cl + Me_3SiCl \xrightarrow{-HCl} R-\underset{\underset{SiMe_3}{|}}{N}-\overset{\overset{O}{\|}}{C}-Cl \rightarrow RNCO + Me_3SiCl$$

Actually it was found, however, that little or no substitution at the nitrogen–hydrogen bond with evolution of gaseous hydrogen chloride takes place even when trimethylsilyl chloride, triethylsilyl chloride, silicon tetrachloride, etc. are heated with methylcarbamoyl chloride at 90°C for a long time. It was thus established that carbonyl chloride attacks $RNHSiR'_3$ by rupturing the N–H bond, not the Si–N bond, and by forming *N*-trialkylsilylcarbamoyl chlorides as intermediate products:

$$R-\underset{\underset{H}{|}}{N}-SiMe_3 \xrightarrow[-HCl]{COCl_2} R-\underset{\underset{SiMe_3}{|}}{N}-\overset{\overset{O}{\|}}{C}-Cl \xrightarrow{-Me_3SiCl} R-N=C=O$$

The high yields of isocyanates at low temperatures of treatment with carbonyl chloride are explained by the thermal instability of the silylated carbamoyl chlorides due to the σσ-conjugated bond system Si–N–C–Cl for even below room temperature they undergo β-elimination with separation of isocyanate and trialkylchlorosilane molecules. A similar tendency to β-elimination is exhibited[178] by the well studied systems of the type Si–C–C–Y (where Y = Hal, OH, etc.).

The ease of thermal cleavage of *N*-silylcarbamoyl chlorides is especially marked in comparison with related compounds containing an analogous Si–N–C–X bond system but with different X substituents (X = OR, where R = Alk, Ar). In the case of *N*-silylurethanes, for example, containing the $\gtrdot$Si–NR′–CO–OR fragment, the tendency to β-elimination becomes much stronger on passing from alkoxy- to aryloxy-derivatives[94,179]. Replacement of OR by the more electronegative Cl intensifies σσ-conjugation still more, and enhances the thermal instability of *N*-silylcarbamoyl chlorides in comparison with *N*-silylurethanes. Furthermore, since chlorosilanes do not react with isocyanates, breakdown of the *N*-silylcarbamoyl chlorides is an irreversible stage, which is another important reason for the high yield of isocyanates at low temperatures of treatment with carbonyl chloride.

The method of preparing organic and organosilicon isocyanates by treating silylamines with carbonyl chloride was extended to *NN*-disilylamines of type $R.N(SiR'_3)_2$. The silicon–nitrogen bonds in these compounds are easily broken even at temperatures below 0°C with formation of an isocyanate and a chlorosilane[94,173-176]:

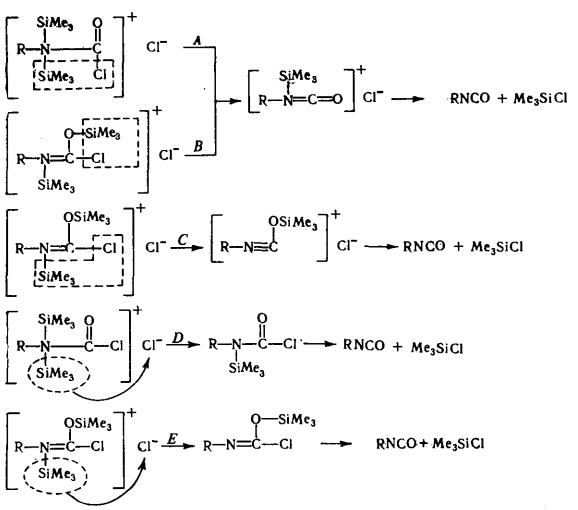
$$RN(SiR'_3)_2 + COCl_2 \rightarrow RNCO + 2R'_3SiCl$$

In this case the yield of saturated and unsaturated aliphatic, aliphatic–aromatic, and purely aromatic isocyanates, including those containing organosilyl substituents, approaches theoretical.

The mechanism of the reaction of silylamines with carbonyl chloride probably involves initial formation of an adduct resembling the complexes of tertiary organic amines with carbonyl chloride[180] and having the structure of an imidate with two equivalent and equally polarised silicon–nitrogen bonds. In considering the mechanism of the breakdown of such a salt we must take into account its possible existence in the tautomeric *O*-form (by analogy with *NN*-bistrimethylsilylamides of carboxylic acids[81])

$$\left[\begin{array}{l} Me_3Si \\ R-N \\ Me_3Si \end{array}\!\!-\!\!\overset{\overset{O}{\|}}{C}\!\!<_{Cl}\right]^+ Cl^- \rightleftharpoons \left[\begin{array}{l} OSiMe_3 \\ R-N=C-Cl \\ Me_3Si \end{array}\right]^+ Cl^-$$

and also the possibility that the first stage of breakdown may involve a chlorine atom either in the inner sphere of the molecule (reactions *A*–*C*) or in the outer sphere (reactions *D* and *E*):



At present it is difficult to say what is the true course of the reaction. In view of the greater tendency of the Si–N–C–X bond system than of Si–N=C–X to undergo β-elimination, however, mechanism *C* can be regarded as the least probable. The other four paths are equally probable, although ionic chlorine is probably more active.

Small quantities of carbamoyl chlorides and amine hydrochlorides are formed as side-products in the reaction of *N*-monosilylamines with carbonyl chloride. Formation of the carbamoyl chlorides is due either to some reaction at the silicon–nitrogen bond or to the addition of incompletely removed hydrogen chloride to the isocyanate. Amine hydrochlorides result from cleavage of the initial silylamine or the silylated carbamoyl chloride by hydrogen

chloride. The formation of secondary products can be reduced to a minimum by conducting the reactions in solvents which only weakly retain hydrogen chloride or in the absence of a solvent, by adding the silylamine to the carbonyl chloride, and by keeping the temperature conditions as mild as possible. The action of carbonyl chloride on disilylated organic and organosilicon amines is unambiguous.

The amino-group can be protected not only with trialkylsilyl groups R_3Si- but also with other groups such as $R_2Si=$, $RSi\equiv$, and $=S=$, as well as incompletely substituted silyl groups.

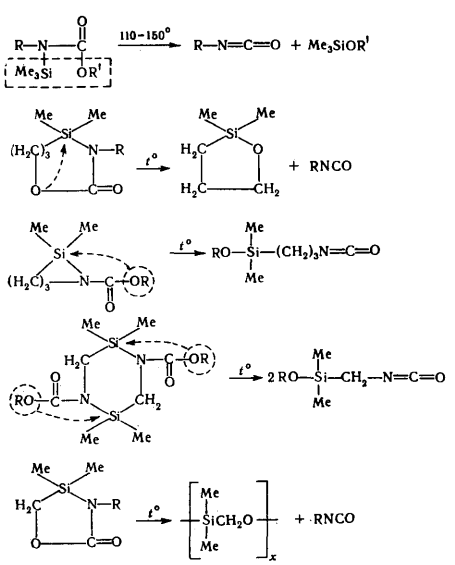
Thus the method of treating *N*-mono- and *NN*-di-silylamines not only simplifies the preparation of organosilicon isocyanates but also enables compounds to be obtained whose preparation is difficult or impossible without silyl protection. For example, it has recently been shown that this method is extremely convenient for preparing esters of *N*-carbonyl-α-amino-acids [181]. Since the production of silylamines is a simple operation, and the silicon-containing fragment is completely regenerated during treatment with carbonyl chloride, this method of obtaining isocyanates shows great industrial promise.

(*e*) Pyrolysis of esters of silicon-containing carbamic acids

The characteristic thermal decomposition of carbamic esters to isocyanates has proved entirely suitable for the preparation of organosilicon isocyanates, including those with alkoxy-groups attached to the silicon atom. The reaction is reversible, and the alcohol must be removed from the reaction mixture for complete conversion of the urethane into the isocyanate [94,182]:

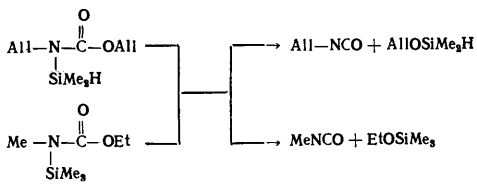
$$R_n(R'O)_{3-n}Si(CH_2)_mNHC(O)OR'' \xrightarrow{t^\circ} R_n(R'O)_{3-n}Si(CH_2)_mNCO + R''OH$$

N-Silylated urethanes show a greater tendency than the unsubstituted compounds to decompose. This is probably due to the irreversibility of cleavage of the σσ-conjugated bond system $\geqslant$Si–N–C–OR. This is a general reaction [94,179,183–189] and can be successfully used for the preparation of various organic and organosilicon isocyanates: e.g.



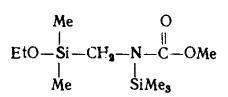
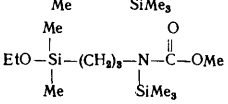
where R is an organic or organosilicon group.

When two urethanes having different *N*-silyl substituents and different alkoxy-groups undergo pyrolysis together, no alkoxysilanes of mixed structure are present among the decomposition products [190]:



This shows that no exchange of silyl groups between the urethanes occurs before the β-decomposition, which takes place by an intramolecular mechanism.

Proportions of products of trans-silylation and of β-decomposition from *N*-silyl-*N*-silylalkylurethanes.

N-Silyl-*N*-silylalkylurethane	Alkoxysilane (%) formed by	
	trans-silylation	β-elimination
	Me_3SiOEt 30	Me_3SiOMe 70
	Me_3SiOEt 87	Me_3SiOMe 13

The composition of the pyrolysis products from specially prepared compounds indicates that the β-elimination of *N*-silylurethanes containing also an *N*-alkoxysilylalkyl group is preceded by trans-silylation [191] (see Table). In contrast to the intramolecular process of β-elimination, trans-silylation can probably occur by both intramolecular and intermolecular mechanisms. The latter mechanism probably predominates in the first example, in view of the difficulty of formation of an azasilacyclobutane derivative, and intramolecular trans-silylation in the second example. The complicating effect of trans-silylation should be taken into account when examining kinetic data on the β-elimination of *N*-alkoxysilylalkyl-*N*-silylcarbamic esters [94,188,192,193].

(*f*) Reaction of silylalkyl halides with metal cyanates

The first attempts to obtain isocyanates by exchange between silylmethyl halides and metal cyanates were unsuccessful [195–197]. Silylalkyl isocyanates have recently been obtained (though in moderate yield) [198–202] by the use of dimethylformamide as solvent:

$$R_3Si(CH_2)_nCl + MOCN \xrightarrow[H.CON(CH_3)_2]{140-150^\circ C} R_3Si(CH_2)_nNCO + MCl\ .$$

($n = 1.3$; M=K, Na)

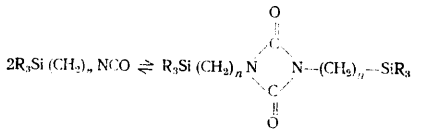
The effects of temperature, nature of solvent, and reactant and catalyst concentrations on the rate and the direction of the exchange between trialkylsilylalkyl chlorides and potassium cyanate have been examined [182,203–206]. This indicated that the optimum conditions for the preparation of silylalkyl isocyanates in dimethylformamide involve equimolecular proportions of 0.6 M silylalkyl

chloride and potassium cyanate with 5% (on weight of salt) of tetra-alkylammonium iodide as catalyst at 150°C for 20 min, when the yield of isocyanate reaches 60–70%.

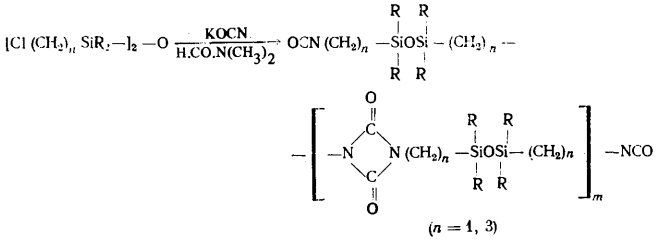
When the time of contact between the reactants is increased to 2–3 h, only dimeric products are formed [94,203–206]. The alkali-metal (sodium or potassium) cyanates used catalyse the dimerisation. Pyridine, triethylamine, and phenyldiethylphosphine also catalyse this reaction. Salts such as potassium, sodium, and tetra-alkylammonium chlorides and tetra-alkylammonium iodides present in the reaction mixture have no catalytic effect.

Replacement of potassium cyanate by the sodium salt has no significant effect on the yield of silylalkyl isocyanate although the duration of the preparation is increased [205]. Silylalkyl isocyanates are not formed in the absence of a solvent, in such solvents as benzene, acetone, and acetonitrile (probably because of the sparing solubility of potassium cyanate), nor in the presence of excess of the initial silylalkyl halide. 3-Chloropropylsilanes are rather less reactive than the chloromethyl derivatives in the exchanges, which is explained by the possible participation of *d*-orbitals of the silicon atom in formation of the intermediate complex in the case of α-derivatives [203].

A dioxouretidine structure was assigned to the dimeric form of the silylalkyl isocyanates, at first conjecturally [166] and then on the basis of infrared spectra [204]. Dimeric and monomeric forms are present in equilibrium [94,204]:



Bishalogenoalkyldisiloxane derivatives form with potassium cyanate in dimethylformamide mainly oligomeric and polymeric products having terminal isocyanato-groups (together with small quantities of the monomeric di-isocyanates) [182,202–205,207]:



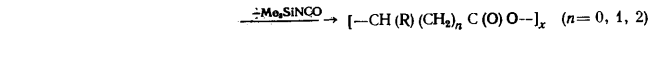
($n = 1, 3$)

When the initial mixture of reactants is heated for 20–30 min, di-isocyanates cannot be isolated at all, since only polymeric products are formed.

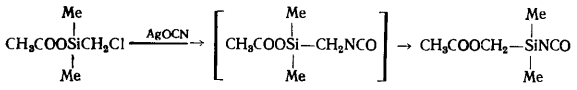
(*g*) Other reactions

A number of other chemical reactions of organosilicon compounds have been described, in which isocyanates are quite often formed only as intermediate products. These reactions can be briefly illustrated by the following schemes.

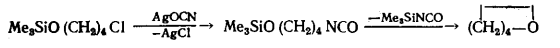
1. Decomposition of products of the reaction of trimethylsilyl α-, β-, and γ-bromo-carboxylates with silver cyanate [208]:



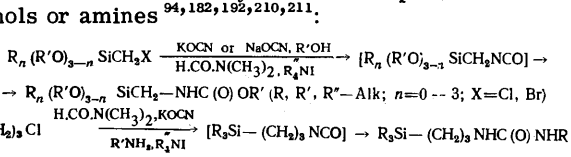
2. Isomerisation of an isocyanatomethylsilane into an isocyanatosilane [208]:



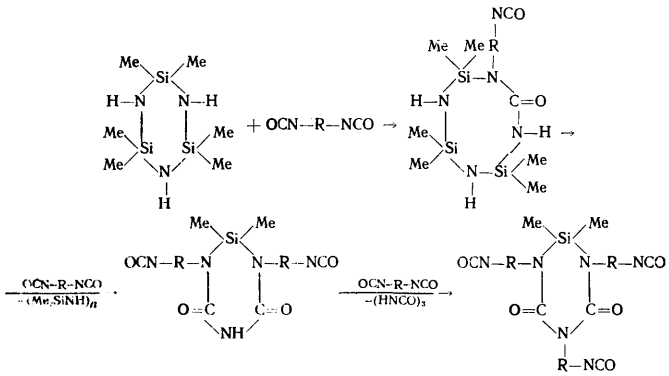
3. δ-Elimination from 4-siloxybutyl isocyanates [208] (in contrast to the stable tetrakisisocyanatomethoxysilane [209]):



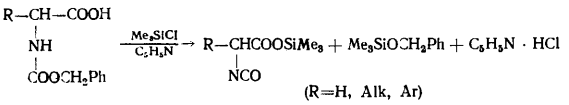
4. Formation of urethanes and ureas when silylalkyl halides react with metal cyanates in the presence of alcohols or amines [94,182,192,210,211]:



5. Interaction of hexamethylcyclosilazanes with excess of a di-isocyanate [212]:

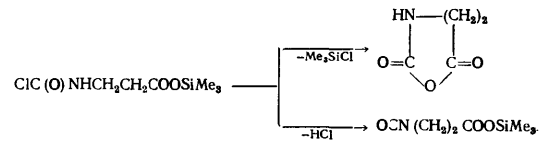


6. Decomposition of derivatives of organic amino-acids with strong silyl protection [185,186]:

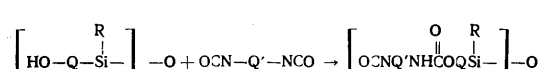


(R=H, Alk, Ar)

7. Interaction of bistrimethylsilyl α-azaglutarates with thionyl chloride, carbonyl chloride, or a phosphorus trihalide [213]. Isocyanates are formed as side-products in this reaction, which yields predominantly amino-acid anhydrides:

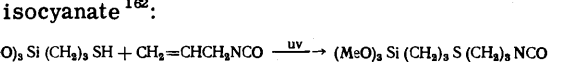


8. Addition of silicon-containing organic diols to di-isocyanates [214]:

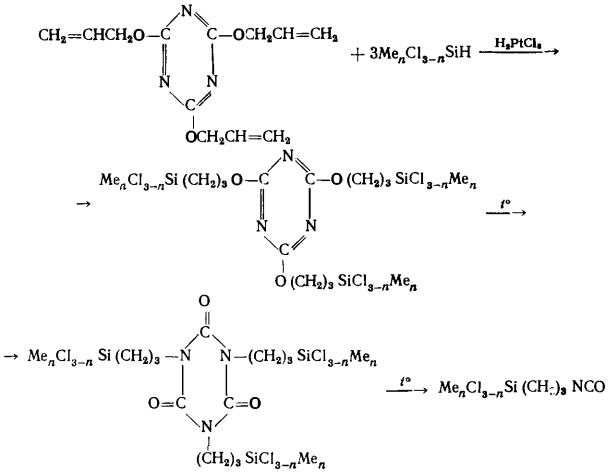


(R=Me, R'=Ph; Q=—$(CH_2)_4$—, Q'=—$(CH_2)_6$—, —MeC_6H_3—)

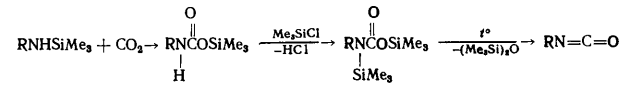
9. Addition of silylalkanethiols at the double bond of allyl isocyanate [162]:



10. Pyrolysis of products of the hydrosilylation of triallyl cyanurate [94]:



11. An interesting method for obtaining organic and organosilicon isocyanates avoids the use of carbonyl chloride [215]:



(*h*) Oligomeric and polymeric silylalkyl and silylaryl isocyanates

A great deal of information has been published on oligomeric and polymeric organosilicon *C*-isocyanates, chiefly in the patent literature. These compounds can be formed in principle by the following processes—(i) hydrosilylation of alkenyl isocyanates with oligo(or poly)siloxanes having terminal Si–H bonds [159], (ii) chain termination in polysiloxanes by ω-isocyanatoalkylsilanes [216], (iii) treatment of siloxanes having terminal hydroxyalkyl and other groups with excess of an organic di-isocyanate [217–221], (iv) reaction of excess of an organic di-isocyanate with hydroxyl containing unsaturated compounds followed by addition of incompletely substituted silanes at ethylemic bonds [158,159], (v) action of excess of an organic di-isocyanate on silocanes having terminal aminoalkyl groups [218], (vi) condensation of organosilicon alcohols with organic or organosilicon di- or tri-isocyanates [167,214,217,220], (vii) pyrolysis of adducts of oligosiloxanes (having terminal aminoalkyl groups) with phenyl chloroformate [159], (viii) interaction of excess of an organosilicon di-isocyanate with silazanes and cyclosilazanes [212,222], (ix) stepwise action of carbonyl chloride on oligosiloxanes containing terminal amino-groups [169,223–225], and (x) synthesis of polyisocyanates from 1,3-bis-ω-chloroalkyldialkyldisiloxanes and alkali-metal cyanates [206].

2. Physical Properties

Monomeric and oligomeric organosilicon *C*-isocyanates are colourless or slightly yellowish liquids, indefinitely stable in the absence of moisture but easily hydrolysed in moist air [94,159,170,207]. When heated to 150–200°C, monomeric di-isocyanates form oligomeric products having terminal isocyanato-groups [207].

The infrared spectra of monoisocyanates [94,162,185,186,204,214,226] contain an intense absorption band due to the isocyanato-group in the range 2267–2243 cm^{-1}. A similarly intense bond has been observed with di-isocyanates (2270–2243 cm^{-1}).

The nuclear magnetic resonance spectra of several mono- and di-isocyanates have been discussed in Ref. 94.

3. Chemical Properties

Like their carbon analogues, silicon-containing isocyanates react vigorously with ammonia and with primary and secondary amines to form silicon-containing ureas [94,154,163,203,227], and with hydrazides and amides of carboxylic acids to give the corresponding semicarbazides [203,226] and acylureas [203]. Urethanes and symmetrical ureas respectively are obtained with alcohols and with water [94,154,203,228].

Silicon-containing di-isocyanates on treatment with ammonia and with primary and secondary amines can be converted into the corresponding bisureas, and by the action of *NN'*-dialkylhydrazines into the bis-semicarbazides [94,173,207,229–234]. Reaction of the di-isocyanates with organic diamines or hydrazines yields polysilylalkylureas or polysilylalkylsemicarbazides [235–237].

Various reagents containing a mobile hydrogen atom form the sequence

amines > hydrazides ≫ water > alcohol > amides

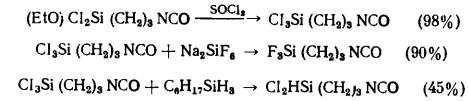
according to their reactivity towards 3-triethylsilylpropyl isocyanate [226]. The reactivity of an isocyanate of type $R_3Si.[CH_2]_nNCO$ with $n = 3$ exceeds that of the compound having $n = 1$ about twentyfold [226].

Heating converts silicon-containing aromatic isocyanates into carbodi-imides:

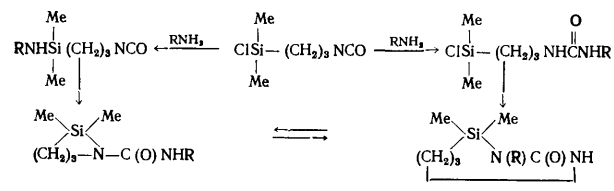


This reaction is catalysed by phosphorus compounds such as phosphafluorene. The aliphatic isocyanates do not undergo this reaction. In the presence of amines, amides, sodium benzoate, and other basic catalysts they form isocyanurates [238,239].

Several reactions of silylalkyl isocyanates have been described that do not involve the isocyanato-group [169,240]:



Chloro- and alkoxy-silylalkyl isocyanates exhibit dual reactivity. With water, for example, they give siloxane di-isocyanates [94,177], but with more active reagents (amines) with functional groups are involved [241]:



The isocyanato-group is also extraordinarily reactive in oligomeric compounds of silicon, and reacts with all types of reagents containing active hydrogen atoms [159].

4. Prospects for the Application of Silicon-containing C-Isocyanates

The enhanced interest taken in silylalkyl isocyanates is due primarily to the possibility of obtaining from them cold-self-vulcanising polysiloxane rubbers and polyurethanes with improved resistance to heat, moisture, and frost[159,218,221]. Cold vulcanisation takes place under normal conditions; the only byproduct is carbon dioxide, which readily diffuses through the vulcanised product. These rubbers contain carbamide cross-links, and surpass in mechanical strength and resistance to oils and benzene their alkoxylated and acyloxylated organosilicon analogues. They differ advantageously from ordinary polyurethane rubbers in high moisture resistance and in low-temperature elasticity[135,136,142,159,218,219].

Polymeric materials based on silicon-containing organic isocyanates can be used for the manufacture of various articles by moulding and casting, as insulating materials, for coating electrical goods, and for other purposes. The ability to set at low temperatures enables them to be employed e.g. for treating sensitive materials such as leather, paper, and cloth, in the printing industry, as sealants, etc.[159,169,218]

Silicon-containing organic di-isocyanates have been proposed for the production of polyurethane, polyurea, polyamide, etc. materials[159,207,218,220,221] and also for the synthesis of polysiloxane polymers containing free isocyanato-groups. The latter have been used to obtain plastics, rubbers, resins, liquids, and films[159,170,218,242]. Information has been published on the use of silanes and siloxanes with isocyanato-groups in the radical as hydraulic fluids, rubbers, elastomers, and adhesives[169,243] and for conferring wear resistance on polyamide and polyester fibres, and water resistance and adhesion on coatings[244].

Silicon-containing organic polyisocyanates improve the adhesion to substrates of hardenable compositions such as as silicones, polyacrylates, polyurethanes, and polysulphides[167,245,246]. Silanes and siloxanes modified with isocyanate fragments can be employed to obtain film coatings[156,162,202,246], rubbers, and resins[246], for impregnating various materials in order to confer water-repellent properties[158,182,224,247], as glues[248], surface-active agents[248], foam stabilisers in the production of polyurethane foams[223,249], for cementing glass[162,174], and for other purposes[159,160,167,212,216,242,243,249-253].

Research is probably widely developed on the application of organosilicon compounds mixed with organic isocyanates (with the components chemically uncombined in the initial mixtures). Combinations of organopolysiloxanes with organic di-isocyanates have already been suggested as coatings for electrical goods, distinguished by high heat resistance, elasticity, good adhesion to metals, and improved insulating properties compared with the usual polysiloxane varnishes[254].

Combining polysiloxanes with a mixture of polyesters and di-isocyanates yields compositions which foam at relatively low temperatures without the use of blowing agents[255] and are stable when heated to 200–250°C.

Rubberlike polymers based on silanediols and organic polyesters with terminal isocyanato-groups are elastic, durable, and heat-resistant[256].

Treating fillers for silicone rubber with organic polyisocyanates tends to reinforce them[257,258], and the application of mixtures of organosiloxanes or hydrolysable organosilanes with organic isocyanates to natural or synthetic materials confers hydrophobic properties on them[259].

Organic and organosilicon compounds mixed with isocyanates either individually or as components of more complicated compositions have been proposed for the preparation of water-repellent lubricating greases[260,261], elastic fibres[262], and adhesives[263], as well as for many other purposes[264-268].

Organic isocyanates have been patented as quick-setting agents for liquid organosilicon oligomers, polymers, and copolymers[269,270]. Compositions based on silicones containing isocyanato-groups and purely organic di- and polyfunctional compounds will apparently be identical in properties with materials based on organic di- and polyisocyanates and carbofunctional polysiloxanes. Since polymers of the latter type are unrelated to the topic of the present Review, we will merely list references to this work[271-293]. Investigations have been made also on polymeric materials based on organic isocyanates in which the organosilicon component has a subordinate role (surface-active agents, fillers, pore-regulators, stabilisers, catalysts, adhesion additives, etc.[294-304]).

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Stereochemical Non-rigidity (Internal Rotation and Metallotropy) of Organic Derivatives of Transition Metals Investigated by Nuclear Magnetic Resonance Spectroscopy

L.A.Fedorov

Types of stereochemical non-rigidity of organic derivatives of transition metals, which have been widely studied by nuclear magnetic resonance during recent years, are classified. Two types of process—internal rotation in complexes of transition metals and intramolecular transfers of metal-containing groups (metallotropy)—are examined in greater detail. The discussion of the most characteristic structural situations met in π-complexes of transition metals covers not only the dynamic processes already observed by the n.m.r. method but also examples of compounds for which such processes have not yet been observed but may in principle be found. A list of 256 references is included.

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I. INTRODUCTION

With many organometallic structures two aspects—static and dynamic—must be considered. The dynamic aspect implies possible activation of molecular rearrangements which cannot be classified as oscillations. Although this problem has been posed and solved for organic chemistry during the past few decades, for organometallic and inorganic chemistry it has become urgent only during recent years.

Many of the known types of dynamic processes can be examined by nuclear magnetic resonance. Some of them are intermolecular, and n.m.r. is widely used for their study (see e.g. reviews on intermolecular dynamics† in organometallic derivatives [1-6]). Other types of processes are intramolecular, and are a kind of manifestation of the "stereochemical non-rigidity" of the compounds (this term was proposed by Muetterties [7]). In several organometallic compounds transitions occur between non-equilibrium states of the system (non-degenerate conversions). In other compounds the intramolecular conversions are degenerate, so that the final state is indistinguishable from the initial state of the system. Nuclear magnetic resonance is an especially fertile approach to such systems, since the actual fact of conversion and also its mechanism cannot always be detected and studied by other methods.

† In the papers under discussion the word "dynamics" is applied to any processes which either lead to or are accompanied by a change in the relative equilibrium arrangement of the atoms in the molecule.

1. Types of Intramolecular Transitions

Nuclear magnetic resonance has been used to study many types of intramolecular processes in organic derivatives of transition metals. However, certain especially characteristic and quite frequent processes—internal rotation, tautomeric transitions, allogonic rearrangements (pseudorotation), reconstruction of organometallic rings, etc.—can be distinguished. Nevertheless, "purely" intramolecular processes are almost impossible under the actual conditions of an n.m.r. experiment, owing to the effect of the solvent and similar factors. It is therefore necessary to determine which processes can be regarded as intramolecular. We shall apply the term *intramolecular* to processes which do not involve breakdown of the compound into two or more kinetically independent species or entry of the compound into other kinetically independent species (stable solvates, complexes.

With internal rotation a change in the orientation of one fragment relative to another in a compound is accomplished by turning about an axis coinciding in direction with a chemical bond. In contrast to traditional organic compounds, internal rotation in transition-metal complexes can occur not only about a localised (σ or coordinate) bond but also about delocalised π-bonds, including bonds of order exceeding unity.

Tautomeric processes in organometallic compounds of transition metals involving intramolecular rearrangements

of metal-containing groups (metallotropic transitions) are fundamentally novel and therefore especially interesting. Metallotropic transitions occur in any change in the relative positions of two fragments of the compound—the metal (or metal-containing group) and the remainder of the molecule—which is accompanied by a redistribution of its bond system. Metallotropy was first studied by Nesmeyanov and Kravtsov on the intramolecular migration of a transition metal between σ-bonds in a compound [8]. Since then examples have also been found of various migrations of metal-containing groups on π-complexes of transition metals. The richness and variety of the structural possibilities characteristic of transition-metal complexes result in a multiplicity of types of metallotropic transitions.

Allogonic rearrangements (pseudorotation) cover all processes occuring in coordination polyhedra (including square planar complexes and complexes containing *inter alia* different kinds of π-bonds). They include also rearrangements of the skeleton of coordination compounds in which a polyhedron different from the original is formed as transition state (pseudorotation, a term proposed by Berry [9]) or intermediate (allogonic rearrangements, a term proposed by Bennett et al. [10]).

The stereochemical non-rigidity of organometallic rings containing the metal in the main skeleton of the ring may involve both the dynamic aspects that are investigated on the usual organic rings and several questions specific to organometallic compounds, such as the possibility of intermediate opening of the ring, etc.

The history of the problem is comparatively brief. During the "preparatory" decade 1956–1966 the efforts of various workers [7-27] led to the discovery and the investigation of several types of intramolecular conversions in organometallic compounds, and also in a series of compounds which can be regarded as models for organometallic structures. Thus the main outlines of the problem were revealed, and certain hypotheses formulated on the mechanisms of the molecular reorientations. A period of "attack and charge" began in 1967, characterised by an avalanche of fresh information. No tendency is yet evident for this process to level off on a plateau.

Thus, in spite of the relative novelty of the problem, the literature on the stereochemical non-rigidity of organometallic compounds is so large that it is already quite difficult to cover in a short survey (Cotton's review was published in 1968, [28] and that of Vrieze et al. in 1969 [5]). Only the first two types of intramolecular dynamics—internal rotation and tautomerism—will therefore be discussed in the present Review. However, we must not ignore the formality of any such (including the suggested) classification of these processes and hence the difficulty of deciding in several cases what type of transition takes place in a particular molecular system.

2. Equivalence of Nuclei in Static Molecule

Following Abragam's suggestion [29] comparable nuclei are termed *isochronous* if they have the same shielding, and *anisochronous* if their shielding differs. Nuclei may be either regularly or accidentally isochronous. Isochronous nuclei are equivalent only if their equivalence is due to considerations of symmetry (static or dynamic). Otherwise they are non-equivalent even if a spectroscopic experiment indicates identity of shielding (accidentally isochronous).

Depending on their relative arrangement in the molecule any comparable groups—by which we shall henceforward imply comparable nuclei or groups of nuclei in some fragment—may be either chemically equivalent, enantiotopic, or diastereotopic. Groups which are coupled by a simple axis of rotation C_n ($1 < n < \infty$) are chemically equivalent [30]. Groups that are defined as chemically equivalent, and hence isochronous "from the viewpoint" of nuclear magnetic resonance spectroscopy, are in fact equivalent in chemical terms: i.e. they cannot be distinguished by their behaviour in any chemical reaction [31] and they cannot become spectroscopically distinguishable in a chiral medium. Enantiotopic groups possess an enantiomeric environment and hence are coupled by a reflection–rotation axis S_n (rotation about axis C_n followed by reflection in the plane of symmetry, $1 \leq n < \infty$). [32] Enantiotopic groups are isochronous in achiral (optically inactive) solvents, but may become anisochronous in chiral media. Finally, diastereotopic groups cannot be interchanged by any symmetry operation, and thus are geometrically non-equivalent [32]. As a consequence, diastereotopic groups should in principle be anisochronous in any solvent. Although the diastereotopy (geometrical non-equivalence) of groups is in principle a necessary condition for the spectroscopic non-equivalence of their nuclei, this condition is not sufficient. Differences in the shielding of diastereotopic nuclei depend on the structure of the molecules, the solvent, and several other factors. In individual cases these differences may become so small that they cannot be observed, and the groups can then be regarded as accidentally isochronous (but not equivalent).

3. Dynamic Equivalence of Nuclei—Dynamic n.m.r. (d.n.m.r.)

The above definitions apply to molecular statics, in which molecules are considered in fixed structural situations with the mutual arrangement of their atoms and bonds unchanged. Actually the investigator is usually dealing not with static but with dynamic stereochemistry. Various intramolecular movements in compounds produce an averaging of the shielding and other spectral parameters of the groups. The symmetry of the molecule seems to improve, and hence the spectrum to degenerate. As a consequence of the degeneracy diastereotopic groups may become "dynamically chemically equivalent" or "dynamically enantiotopic". Several factors—temperature, nature of solvent, concentration of compound, etc.—may in principle be the averaging agent, introducing dynamic equivalence (in the n.m.r. sense) into the molecular system, but the temperature has the greatest importance for intramolecular processes.

The relative character of the "dynamic" behaviour of molecular systems must be emphasised: particular groups may be diastereotopic for some methods, but chemically equivalent or enantiotopic (dynamically) for others. Thus a spectroscopic examination of a compound usually yields not its absolute but its effective (average) symmetry, and hence the effective equivalence of its groups—equivalence "in terms of" the method of investigation used.

The relative character of the boundary between the static and the dynamic behaviour of a molecular system is governed also by the individual features of the compound (or process) and by the possibilities—the time scale—of the physical method used. A compound may "appear" static, immobile for some methods and dynamic for

others, and the process may correspondingly be "slow" for some methods and "rapid" for others.

The time scale of a spectroscopic method (the time necessary for the observation of discrete spectra) is directly related to the energy of the transitions observed: the smaller the energy of transitions between states of the system, the slower the processes "visible" by this method. A comparison made by Muetterties [7] shows that microwave spectroscopy, particularly high-resolution nuclear magnetic resonance, is substantially "slower" than diffraction methods of analysis, or electronic and vibrational spectroscopy. With processes so rapid that the system remains for $10^{-13}-10^{-15}$ s in each state vibrational spectroscopy, for example, enables the spectrum of each state to be observed, whereas n.m.r. spectroscopy reveals only spectra averaged over several states of the molecular system. On the other hand, n.m.r. spectroscopy enables processes having a lifetime of $10^{-1}-10^{-9}$ s to be observed, and is quite rapid in comparison with any method involving direct isolation of molecular systems in any discrete states (if these states are non-degenerate, and such separation is feasible).

Thus n.m.r. spectroscopy is a fortunate method of investigation for chemistry, since it is able to cover a range of processes and problems which are often inaccessible to other methods. These include various states of organometallic compounds and their reactions having activation energies of 5–25 kcal mole^{-1}. This is especially important because the molecular structure of these compounds in the liquid phase may differ from their structure in the crystal [7]. The branch of n.m.r. spectroscopy used to investigate the inter- and intra-molecular dynamics of molecules is termed dynamic nuclear magnetic resonance (d.n.m.r.). Beginning with the classic work of Gutowsky and his collaborators [33-35], this branch underwent serious theoretical development and has found many applications (see reviews [36,37]).

Information on the dynamics of a molecule can in principle be obtained also by examining a "frozen" spectrum ("slow dynamics", the indicator groups being dynamically chemically non-equivalent or enantiotopic). However, investigation of a compound is especially fruitful and informative in a critical region, in which a small perturbation (change in temperature, introduction of a somewhat different substituent, etc.) will reveal the whole sequence of changes in the spectrum—from the "frozen" spectrum, through a series of intermediate spectra, to the degenerate spectrum.

Several d.n.m.r. approaches, including the stereochemical non-rigidity of compounds, have been worked out in the investigation of dynamic phenomena. The simplest approach is to study the merging of the signals. The kinetic and thermodynamic parameters are obtained by finding experimentally the coalescence temperature T_c. However, this approach will give acceptable results only for the simplest systems, in particular for a two-centre exchange without spin–spin interaction between the nuclei of diastereotopic groups.

However, complete analysis (usually by means of an electric computer) of the changes in spectral line form accompanying effective averaging of the environments of the diastereotopic groups is required for accurate investigation. Importance attaches both to the "limiting" spectra (the discrete, "static" spectrum, and also the averaged, "dynamic" spectrum) and to all intermediate spectra produced as the averaging process gradually becomes more intense. With intramolecular processes, as already mentioned, only changes in the temperature of the solution can act as such an averaging agent.

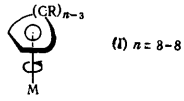
II. INTERNAL ROTATION IN COMPLEXES OF TRANSITION METALS

Rotation about σ-bonds has been relatively well studied on various organic models (e.g. review [38]). This type of dynamics applied to coordinate bonds and metal–ligand σ-bonds has also become the object of n.m.r. investigations during recent years [39-46], although it evidently possesses no special theoretical features.

Studies of two "new" types of rotation—about metal–ligand π-bonds and also in the ligands themselves having a π-type of coordination to a transition-metal atom—give especially interesting structural information. Investigation of this type of dynamics enables the problem of the electronic structure of π-bonds to be discussed from a fresh point of view [47].

1. Rotation about Metal–Ligand π-Bonds

Internal rotation about the n-fold axis in complexes in which a π-C_nR_n–M bond is formed (where C_nR_n is a cyclic ligand in which the multiple bonds are all equivalent and all involved in complex formation, $n = 3-8$, and R = H or R ≠ H—structure I)

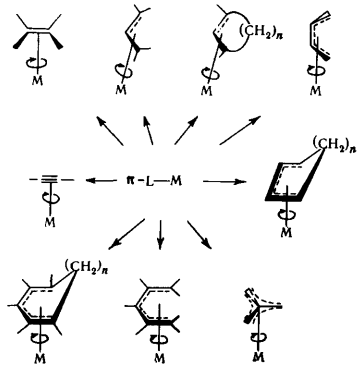


(I) n = 3-8

is opposed by such low barriers that its rate evidently cannot be measured by high-resolution n.m.r. in solution (see e.g. Refs. 48–51 for $n = 5$ and 6). With complexes in which the multiple-bond system coordinated with the transition-metal atom is not continuous, or else is continuous but non-uniform, on the other hand, examination of internal rotation is in many cases "permitted" by the high-resolution n.m.r. time scale. The first study of this kind was made by Cramer [15].

Scheme 1

Some possible types of internal rotation about metal–ligand π-bonds



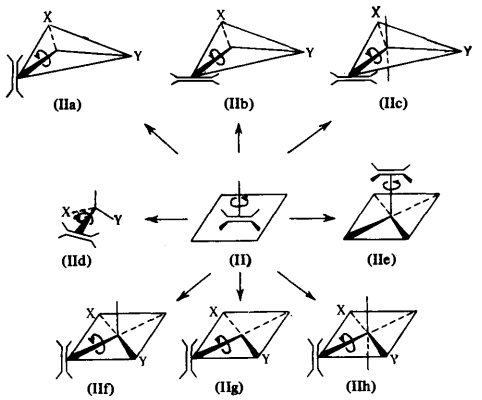
Among the main types of structures (Scheme 1) that can be examined in connection with the problem of internal rotation about a metal–ligand π-bond, π-ethylenic and π-allylic derivatives have been most studied.

(*a*) Internal rotation in π-ethylenic complexes

Various criteria can be used in examining internal rotation about a π-alkene–metal bond in π-ethylenic derivatives (structure II), the choice of which depends on the symmetry of the whole complex (i.e. on whether its rotational isomers are equivalent or non-equivalent). Scheme 2 assembles several types of π-ethylenic complexes, on which the problem of internal rotation can conveniently be considered.

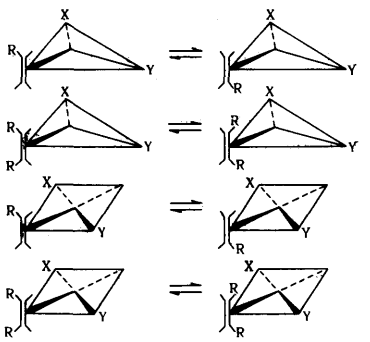
Scheme 2

Some types of structures in which internal rotation about a π-alkene–M bond is possible



Complexes containing highly symmetrical ethylenic ligands [C_2H_4, C_2F_4, $C_2(CH_3)_4$, etc.] and different groups X and Y (structures II—a, g, h), for example, form equivalent rotational isomers. Changes in the rate of degenerate internal rotation in derivatives of this type can conveniently be assessed from the temperature dependence of the ^1H and ^{19}F n.m.r. spectra of the olefinic ligand. At sufficiently low temperatures with "slow" rotation the indicator groups of this ligand (the ^1H and ^{19}F nuclei) separate into two types of diastereotopic nuclei according to their environment and hence shielding. Thus the low-temperature limiting spectrum of the ethylenic ligand does not exhibit a solitary signal (as in the spectrum of the uncomplexed unsaturated compound—the spin system A_4 for ethylene and tetrafluoroethylene, and A_{12} for 2,3-dimethylbut-2-ene) but a set of signals of the system AA'BB' or AA'KK' for the first two compounds, and also the doublet $A_6 + K_6$ for the third compound. Rise in temperature and acceleration of rotation are accompanied by more rapid exchange of the environments of the diastereotopic nuclei and degeneration of the n.m.r. spectrum of the ethylenic ligand ($AA'KK' \rightarrow A_4$, $A_6 + K_6 \rightarrow A_{12}$, etc.).

Rotational isomers of compounds having a ligand of low degree of symmetry (monosubstituted or *cis*-disubstituted ethylene and X = Y are non-equivalent, and each has its own low-temperature boundary n.m.r. spectrum of corresponding intensity. Examination of the temperature dependence of the spectra of such complexes may reveal the interconversion of rotational isomers throughout the range of possible rates—from "slow" to "rapid" dynamics—processes (1)–(4), etc.



The largest number of papers have appeared on internal rotation in complexes of types (IIa) [15,52–58] and (IIg).[59–61] Very few data have yet been obtained on intramolecular dynamics in the other π-ethylenic derivatives—tetrahedral (IId), octahedral (IIh), trigonal bipyramidal (IIc), etc.—included in Scheme 2.[62–67] Low-resolution n.m.r. has also been used for this purpose[68,69].

Application of n.m.r. to rhodium and iridium derivatives of type (IIa) with highly symmetrical π-ethylenic ligands (X = C_5H_5, C_6H_6, etc. and Y = C_2H_4, C_2F_4, SO_2, etc.) shows that the rate of degenerate rotation of the alkene depends significantly on the nature of the metal and on the structure of the rest of the complex. Rotation is appreciably more rapid with M = Rh and Y = SO_2 or C_2F_4 than when Y = C_2H_4. An ethylene ligand (Y = C_2H_4) rotates more slowly in an iridium than in a rhodium complex. A tetrafluoroethylene group rotates much more slowly than does ethylene.

Study of degenerate rotation in platinum complexes PtXAlkeneChelate (X = Cl, Br) of type (IIg) reveals a slight dependence of the rate of rotation of ethylene on the structure of the remainder of the compound. Derivatives of this type also show non-degenerate rotation in the interconversion of isomers obtained from monosubstituted and *cis*-disubstituted ethylenes (reactions (3) and (4) respectively). It is significant that neither substitution of the *cis*-substituent X (Cl by Br) nor replacement of an acetylacetonate by a hexafluoroacetylacetonate ligand produces a definite change in the rate of rotation of the alkene. The very fact of observing geometrical isomers of (IIa) and (IIg) is an unambiguous n.m.r. proof that the axis of the alkene is oriented perpendicular to the plane of the complex both in solution and in the crystal[70,71].

The choice of transition state in the discussion of internal rotation about an alkene–metal π-bond is directly connected with the structure of the complexes. Diffraction data show that in several compounds an ethylenic ligand is oriented perpendicular to the plane of the molecule if such can be distinguished (IIa,[70] IIg,[71] etc.). In these complexes the state in which the ligand lies in the plane of the complex is obviously more favourable energetically, and is observed in the n.m.r. spectrum with slow dynamics, whereas the less favourable transition state is almost unobservable, since its contribution to the spectral parameters is negligible because of its short lifetime. The given dynamics applied to the complexes (IIg) can than be represented by[59]



An attempt was made[59] to assess the effect of electronic and structural factors on the rate of this process and on the stability of its transition state. Since, however, the axis of an ethylenic ligand in a π-complex may be not only perpendicular to but also coplanar with the complex (IIb),[72] the transition state in process (5) may actually be an intermediate complex having an appreciable lifetime and hence making an appreciable contribution to the special parameters.

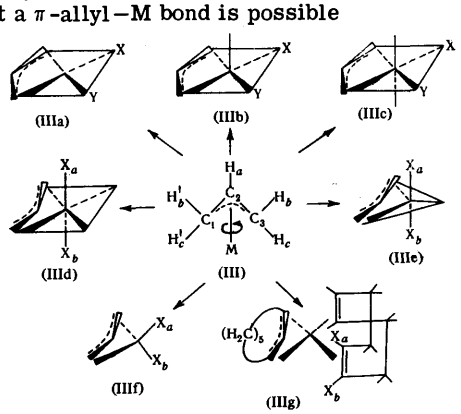
The observation of intramolecular rotation in ethylenic π-complexes by d.n.m.r. may in principle be complicated by a contribution from intermolecular dynamics, connected with the lability of certain alkene–metal π-bonds[73–83]. In several cases, however, experimental conditions can be distinguished which eliminate almost completely the intermolecular component of the process. Criteria of this are, for instance, that the parameters of the n.m.r. spectrum should be independent of the concentration of the compound, additions of the free ligand, etc.[53,76] The observation of spin–spin interaction between nuclei of the ethylenic ligand (hydrogen-1, fluorine-19, carbon-13, etc.) and nuclei of the metal (rhodium-103, platinum-195, etc.) or other ligands (phosphorus-31, etc.) in the π-alkene–metal fragment throughout the range of rates is convincing evidence that the process is intramolecular[15,54,59].

(*b*) Internal rotation in π-allylic complexes

Internal rotation about a π-allyl–metal axis (structure III) can in principle occur quite slowly (on the n.m.r. time scale) in a wide range of compounds in which the metal is attached to a three-electron ligand. Several examples are combined in Scheme 3.

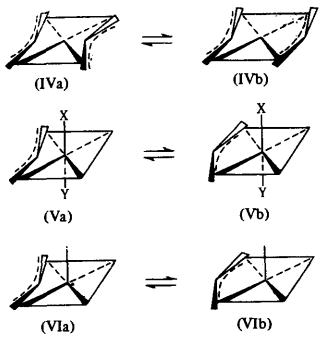
Scheme 3

Some types of structures in which internal rotation about a π-allyl–M bond is possible



Asymmetry in π-allylic complexes with a non-degenerate ligand spectrum of type AGKPX [square planar (IIIa),[84,85] octahedral (IIIc),[86–93] etc.—for terminology see Refs. 91 and 94] originates in the inequality between the substituents X and Y. Slowness of internal rotation in complexes of this type is indicated by the anisochronous behaviour of the terminal methylene groups (structure III)—of the $C_{(1)}$ and $C_{(3)}$ nuclei in the ^{13}C n.m.r. spectrum, and of the *cis*-protons H(b) and H(b′) and also the *trans*-protons H(c) and H(c′) in the ^1H n.m.r. spectrum. With symmetrical complexes (IIId–g), possessing a degenerate spectrum AK_2X_2, slowness of internal rotation is evidenced by anisochronous behaviour of the structurally identical indicator substituents $X_{(a)}$ and $X_{(b)}$, e.g. in the niobium complex (IIIf) [$X_{(a)} = X_{(b)} = \pi\text{-}C_5H_5$ [95]], in the cobalt and rhodium complexes (IIIg),[96,97] etc. [the non-equivalence of the groups $X_{(a)}$ and $X_{(b)}$ is due to the non-coplanarity of the $C_{(1)}–C_{(2)}–C_{(3)}$ and $C_{(1)}–M–C_{(3)}$ planes of the π-allyl–metal bond].

Slowness of rotation about a π-allyl–metal bond may be indicated also by the spectral observation in an appropriate temperature range (and the theoretical possibility of physical separation) of rotational isomers in those types of compounds whose rotamers are non-equivalent from considerations of symmetry. In particular, the isomeric pairs (IV)–(VI) (processes 6–8)



(6)

(7)

(8)

have been observed by ^1H n.m.r. Investigation of the temperature dependence of the ^1H n.m.r. spectrum for several π-allyl compounds of transition metals has shown that internal rotation about the π-allyl–metal bond may occur at rates that can be conveniently recorded by n.m.r. methods. The effect has been examined in greatest detail in a study of molecules of two types—asymmetric π-allylic compounds (IIIc), and also symmetrical compounds forming isomeric pairs (IV)–(VI).

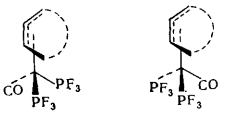
With rise in temperature (dynamic) symmetry appears in the spectrum of the asymmetric complexes (IIIc) (AGKPX → AK_2X_2): anisochronicity of the two terminal methylene groups is replaced by their isochronicity and hence dynamic equivalence. This effect is observed between −20° and 90°C with $[RhCl(\pi\text{-}C_3H_5)_2]_2$,[91] from −67° to 20°C with $Fe(CO)_2(\pi\text{-}C_3H_5)_2$,[88,89] from 60° to 120°C with $Ru(CO)_2(\pi\text{-}C_3H_5)_2$,[93] etc. In the spectra of compounds (IV)–(VI) forming isomeric pairs, interconversion of the rotational isomers (a) and (b) begins to become more rapid with rise in temperature. As a result, the two spin systems AK_2X_2 coalesce into a single system (and the rotational isomers thus become indistinguishable by n.m.r. spectroscopy) or the ratio of the isomers changes[98–102].

With both types of compounds the observed spectral changes are satisfactorily explained on the assumption that the allyl group swings at an appropriate frequency about the metal–ligand axis (process III). The π-allyl ligand thus occupies successively first one and then another orientation relative to the remainder of the molecule, so that the terminal methylene groups exchange their environments [$C_{(1)} \rightleftharpoons C_{(3)}$, H(b) ⇌ H(b′), H(c) ⇌ H(c′)]. A similar explanation applies to the temperature dependence of the spectrum of tri-π-allylrhodium, which probably has a trigonal prism structure[21,22,90]. Becconsall and O'Brien first described intramolecular rotation of type (III) in this particular compound[22]. It must be stressed, however, that the observed spectral changes can in principle be

explained, not by transitions between rotational isomers, but by some other intermolecular (e.g. exchange) or intramolecular (pseudorotation) mechanisms [103]. Thus the most informative spectroscopic methods must be employed to elucidate the true mechanism of stereochemical non-rigidity in these compounds.

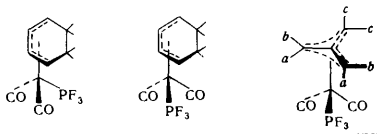
(*c*) Internal rotation in derivatives having four- and five-electron ligands

Internal rotation about the π-C_4H_6–M bond in compounds having four-electron ligands has been investigated on π-butadiene, π-cyclohexadiene, and π-trimethylenemethane complexes of the type π-L–$Fe(CO)_n(PF_3)_{3-n}$. [104-108] The π-butadiene and π-cyclohexadiene derivatives π-$C_4H_6Fe(CO)(PF_3)_2$ and π-$C_6H_8Fe(CO)(PF_3)_2$ can be most conveniently investigated by ^{19}F n.m.r. because of their low degree of symmetry. At sufficiently low temperatures the two trifluorophosphine groups are diastereotopic, but become dynamically equivalent with rise in temperature. These results are consistent with the hypothesis that, of the two non-equivalent rotational isomers



(VIIa) (VIIb)

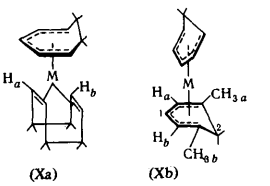
the energetically more favourable isomer (VIIa) is stabilised at low temperatures [104,107]. Investigation of the analogous complex π-$C_6H_8Fe(CO)_2PF_3$ has shown, however, that at low temperatures both rotational isomers—(VIIIa) and (VIIIb)—may exist with closely similar probabilities [107].



(VIIIa) (VIIIb) (IX)

The highly symmetrical π-trimethylenemethane ligand enables the interconversion of rotational isomers to be investigated by proton magnetic resonance. The spectrum of π-$C_4H_6Fe(CO)_2PF_3$ below $-73°C$ contains three equally intense groups of signals corresponding to three types of ligand protons—$H_{(a)}$, $H_{(b)}$, and $H_{(c)}$—in each of the three equivalent rotational isomers (IX). At sufficiently high temperatures, however, the spectrum is a doublet, which indicates the appearance of dynamic equivalence among these protons and the intramolecular character of the dynamics ($^{31}P-{}^{1}H$ spin–spin interaction is observed throughout the temperature range). These spectral changes are attributed [108] to acceleration of rotation about the π-C_4H_6–Fe bond, as a result of which the rotational isomers undergo more rapid interconversion, while the protons $H_{(a)}$, $H_{(b)}$, and $H_{(c)}$ interchange their environments.

A few papers have appeared on intramolecular rotation in complexes containing five-electron ligands. In the cobalt complex which according to n.m.r. data [106] has the "transverse" structure (Xa), the diene protons $H_{(a)}$ and $H_{(b)}$ of the π-cyclo-octa-1,5-diene ligand are diastereotopic owing to the low degree of symmetry of the π-cycloheptadienyl ligand. The temperature dependence of the n.m.r. spectrum shows that these protons are anisochronous at $-25°C$, but become isochronous at $70°C$, obviously as a consequence of dynamic equivalence. These changes in the spectrum were attributed [106] to acceleration of internal rotation about the π-1,5-diene–cobalt bond. However, this is not the only hypothesis, for similar spectral changes should be observed with more rapid rotation about the π-cycloheptadienyl–cobalt bond:



(Xa) (Xb)

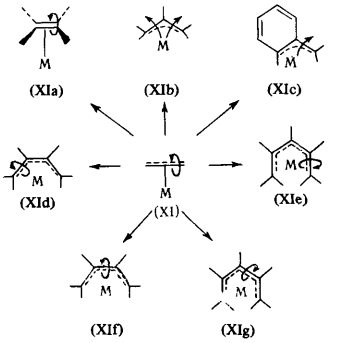
This latter explanation is supported by the temperature dependence of the spectrum of the biscyclohexadienyliron derivative [105]. The low-temperature spectrum of this compound is consistent with the transverse structure (Xb): groups lying outside the plane passing through positions 1, 2, and Fe [$H_{(a)}$ and $H_{(b)}$, $CH_{3(a)}$ and $CH_{3(b)}$] are diastereotopic and anisochronous in the n.m.r. spectrum (the authors [105] interpreted their results somewhat differently). With rise in temperature the shielding of the (*a*) and (*b*) groups averages out, and this is obviously an effect of internal rotation about the metal–pentadienyl π-bond.

2. Rotation about Multiple π-Bonds

In most organic compounds rotation about ethylenic bonds is opposed by considerable barriers, so that n.m.r. has not usually been employed to investigate this type of dynamics (see e.g. review [38]). However, several examples of compounds are known in which these barriers were lowered by certain structural changes, so that internal rotation could be observed by the n.m.r. method [109-118]. Nor is the dynamics associated with rotation about π-bonds with barriers accessible to n.m.r. investigation fundamentally impossible in organic derivatives of transition metals. However, whether or not such dynamics is observable may be determined not only by the structure of the organic ligand but also in considerable measure by the "electronic requirements" of the transition metal. Scheme 4 assembles examples of several structures in which dynamics of type (XI) is theoretically possible.

Scheme 4

Some possible types of internal rotation about multiple bonds in π-complexes of transition metals

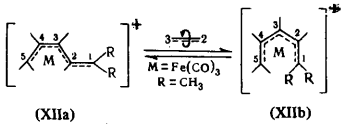


(XIa) (XIb) (XIc) (XId) (XI) (XIe) (XIf) (XIg)

Rotation of type (XIa–e), involving the terminal fragment of a system of multiple bonds, has so far been discussed in connection with n.m.r. data on certain π-allyl (XIb) and π-benzyl (XIc) derivatives. Thus examination of the spectrum of tetra-allylzirconium reveals that the diastereotopic (and anisochronous) *cis*- and *trans*-protons $H_{(b)}$ and $H_{(c)}$, added to each of the terminal carbon atoms (structure III), become isochronous with rise in temperature: whereas the spectrum is of AK_2X_2 type at −74°, it degenerates to AX_4 when the temperature rises to −10°C.[20,98,99,119] A similar spectral pattern is found with tetra-allylthorium (AK_2X_2 at 10° and AX_4 at 80°C).[119] A reversible change in the allylic portion of the spectrum has been found also with π-benzyl derivatives of molybdenum, tungsten, and palladium[19,120,121].

Even in the π-allyl derivatives, however, dynamic equivalence of *cis*- and *trans*-protons has so far been observed only in a limited number of examples. Attempts to detect it in several other π-allylic complexes have proved unsuccessful[91,122,123]. Nor have publications appeared on the dynamics (XI—a, d, e) in other types of π-complexes.

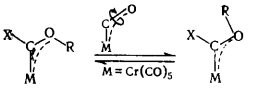
King and Fronzaglia[19], who were the first to observe process (XI) in a π-benzyl compound of molybdenum, suggested that the appearance of isochronicity of the methylene protons with rise in temperature was due to acceleration of rotation about a carbon–carbon bond of order 1.5 in the ligand. The temperature dependence of the spectrum of tetra-allylzirconium has been explained similarly[98]. However, the results obtained are consistent also with alternative mechanisms, including intermediate formation of a σ-type compound[120]:



(XIIa) (XIIb) (9)

The process (XIf, g), involving the central fragment of the system of multiple bonds in the ligand, has been observed only in the derivatives (XIg). Ionic π-pentadienyl complexes of iron exist as two isomers (XII), of which the *cis*-isomer (XIIb) is the more stable[124–127]. Nuclear magnetic resonance has revealed[125] *cis*- and *trans*-interconversions (9) of these isomers at all rates over the whole range, which confirms the possibility that rotation about the 1.5 bond $C_{(2)}–C_{(3)}$ may be accelerated. It is significant that the rate of rotation about the $C_{(1)}–C_{(2)}$ bond is much lower.

Internal rotation in carbene derivatives has been investigated on compounds of type (XIII). At sufficiently low temperatures they exist as two rotational isomers (*trans* and *cis*—XIIIa and XIIIb), each having its own n.m.r. spectrum, including the spectrum of the indicator groups OR (R = CH_3, C_2H_5) and X (X = CH_3, Ar). The relative intensities of the OR (or X) signals show that the mixture contains unequal amounts of the two isomers, which depend on the structure of the compound and the solvating power of the solvent. With rise in temperature the signals of both indicator groups gradually broaden, and then coalesce, at a temperature depending on the nature both of R and of X. An obvious explanation of the observed temperature dependence is that *cis*- and *trans*-isomers may be converted one into the other by internal rotation about the 1.5 bond C·····O:[128–131]



(XIIIa) (XIIIb)

III. INTRAMOLECULAR MIGRATIONS OF METAL-CONTAINING GROUPS (METALLOTROPY)

Processes of several kinds—transition of $\sigma–\sigma$, $\pi–\pi$, and $\sigma–\pi$ types—are included in metallotropy. Migrations of $\sigma–\sigma$ type (sigmatropic transitions) presuppose that the metal forms a localised coordinate or σ-bond with topologically distinguishable ligand atoms before and after the regrouping, during which its system of multiple bonds undergoes rearrangement. Metallotropic systems of this type reproduce formally the corresponding prototropic systems, and transitions can occur both between equivalent and between non-equivalent positions. Transitions of $\pi–\pi$ type consist in transfer of the metal from the system of multiple bonds with which the π-bond was originally formed to another—equivalent or non-equivalent—system. With $\sigma–\pi$ transitions the metal-containing group forms bonds of fundamentally different types with the ligand in initial and final states of the molecule. Transitions of $\pi–\pi$ and $\sigma–\pi$ types have no prototropic analogues.

Metallotropic transitions may be accompanied by either preservation of or change in the "connectedness"‡ of metal and ligand in the metal–ligand fragment of the molecule. The "connectedness" of this fragment is maintained in $\sigma–\sigma$ transitions, but changes during $\sigma–\pi$ transitions. Conversions of $\pi–\pi$ type are more varied: they can take place either with maintenance of or change in the "connectedness" of the given fragment.

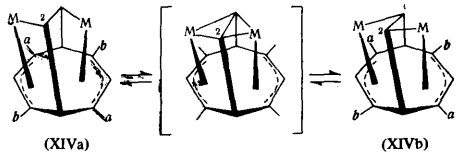
Metallotropic transitions of all the above types will be discussed below with the use of several examples. It must be stressed, however, that there are many organometallic compounds, in particular cluster structures, in which the dynamics is so complicated that it is often difficult to assign to one of the simple types[133–145]. Furthermore, the term "metallotropy" merely indicates the final result of the process—migration of a metal-containing group in space—not its cause or mechanism. These may include the flexibility of the ligand, the ease of formation of the transition state, the spatial proximity of the two energy minima between which the metal-containing group migrates, etc.

1. $\sigma–\sigma$ Transitions

Intramolecular transitions of $\sigma–\sigma$ type, accompanied by rupture of an M–El σ-bond (El = N, O, S, etc.) and formation of a similar or some other σ-bond, have been little studied in the chemistry of transition metals. Only occasional examples are known[146,147]. Intramolecular

‡ The term "connectedness" is the [translation of] the Russian equivalent of *hapto* (proposed by Cotton[132])—the number h^n of the adjacent n atoms of the ligand involved in forming a bond with the metal. This term differs from "denticity" in sense and in range of use, and its application to π-complexes seems justified.

equilibrium $\sigma-\sigma$ transitions of metal-containing groups involving metal–carbon M–C bonds

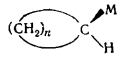


(XIVa) (XIVb)

are obviously of fundamental interest.

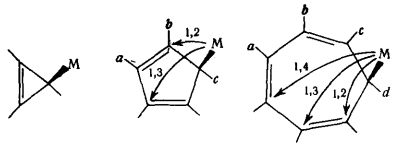
The transformations observed in the n.m.r. spectra of the derivative (XIV) with M = $Fe(CO)_3$ provide an example of such dynamics. Two types of bonds—π-allylic and σ—are formed by each metal atom in this compound. At 0°C the spectrum of the complex corresponds to the low-temperature limiting structure with diastereotopic (and anisochronous) protons $H_{(a)}$ and $H_{(b)}$ in both indicator π-allyl fragments. Gradual changes are observed with rise in temperature, and at 45°C the $H_{(a)}$ and $H_{(b)}$ protons become dynamically equivalent. The cause of these spectral changes is acceleration of the synchronous degenerate transitions of the metal atoms between two possible positions, as a result of which each atom forms a σ-bond alternately with the $C_{(1)}$ atom and with the $C_{(2)}$ atom [148].

In cyclic compounds $\sigma-\sigma$ transitions are most probable in derivatives of the type [28]



(XV) n: a) 1; b) 2; c) 3.

The position of the metal-containing group with respect to the system of double bonds in these compounds is favourable (though in different degrees) for both dynamic and static $\sigma-\pi$ conjugation. This may in principle promote significant activation of the M–C σ-bond, and hence facilitate its dynamics. Among specific examples with $n = 1-3$ σ-cyclopropenyl compounds (XVa) have so far remained completely unstudied, while the largest number of publications are concerned with σ-cyclopentadienyl compounds (XVb):

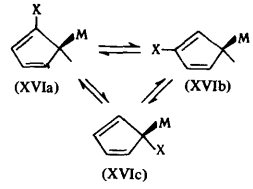


(XVa) (XVb) (XVc)

Dynamic n.m.r. investigation of σ-cyclopentadienyl derivatives of certain transition metals of the iron and chromium subgroups shows that at sufficiently low temperatures the spectrum of the cyclopentadienyl ligand contains a multiplet due to the five-spin system of protons AA'BB'X [10,149–154] (or ABCDX with compounds of lower symmetry [155]; a corresponding set of signals is observed in the ^{13}C n.m.r. spectrum [156]). Such spectra correspond to the presence in these compounds of a localised C_5H_5-M bond, and in several cases this has been confirmed independently by structural investigations by diffraction methods [10,157,158]. A series of patterns of intermediate type is observed with gradual rise in temperature, and at still higher temperatures a single signal representing a situation in which all five ring protons are isochronous owing to the time averaging of their shielding (or for some other reason).

Two main mechanisms have been suggested for the intramolecular migration of a metal-containing group resulting in such averaging: Piper and Wilkinson, the first to meet this phenomenon, pointed to the possibility of $\sigma-\sigma$ transfers of the metal-containing group along the perimeter of the cyclopentadienyl ligand [11]; more recently a mechanism involving a change in type of the C_5H_5-M bond ($\sigma-\pi$ transitions) has been proposed [159]. Either mechanism explains the main features of the ^1H n.m.r. spectra of these compounds. Study of the finer spectral changes shows that, depending on the structure of the compounds and several other factors, both the first [10,152,153] and the second [160–163] (Section III, 2) mechanisms may operate.

Certain features of the mechanisms of $\sigma-\sigma$ transitions in σ-cyclopentadienyl compounds ($\sigma-\pi$ transitions will be considered in Section III, 2) have been studied on derivatives of two types: in compounds containing C_5H_5M fragments (and C_5X_5M in general) migration of the metal-containing group reduces to the degenerate processes



(XVIa) (XVIb) (XVIc) (10)

(where X = H); in derivatives having a substituted ligand (C_5H_4XM, etc.) degeneracy is eliminated, and the process reduces to the interconversion of the isomers (XVI) (X ≠ H). In both cases, however, the $\sigma-\sigma$ transition can in principle involve 1–2 and/or 1–3 migration of the metal-containing group within the cyclic fragment (structure XVb). [10]

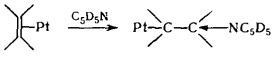
The forms of the $H_{(a)}$ and $H_{(b)}$ signals in derivatives containing a C_5H_5M fragment are found to vary in different rates with rise in temperature (their assignment was based on analysis of the multiplicity of the main signals and their ^{13}C satellites, on the ^{13}C spectra, and also on the proton spectra of corresponding deuteriated derivatives [10,152,153]). The interconversion of isomers of (XVI) has been examined also on a σ-$C_5H_4CH_3$ derivative of ruthenium [153]. These spectral features agree best with 1–2 displacement. Thus a choice could be made in favour of one of the forms of sigmatropic rearrangement—that involving migration of the metal along the shortest path to the adjacent carbon atom (and representing a form of $\sigma-\pi$ conjugation—"counter" dynamics of electrons and metal-containing group). The Woodward–Hoffman rules have also been extended [164] to the mechanism of sigmatropic migration in the derivatives (XVb).

It must be emphasised that a C_5H_5-M σ-bond and hence a $\sigma-\sigma$ mechanism of migration have beem assumed also for many other derivatives—$C_5H_5AuP(C_6H_5)_3$, [165] $C_5H_5(CH_3)_2AuP(C_6H_5)_3$, [166] $C_5H_5(C_6H_5)Pt[P(C_2H_5)_3]_2$, [167] etc. The initial premise in all cases is that the "electronic requirements" of the transition or post-transition metal enable it in principle to form a metal–carbon σ-bond. However, such presuppositions are not sufficieintly convincing by themselves in the absence of other unambiguous confirmation. Such support could come from the detection of the AA'BB'X spin system in the low-temperature ^1H n.m.r. spectrum, the detection of a localised bond when the compounds are examined by diffraction, etc. In any specific case, moreover, additional investigations are

necessary which would reveal some disregarded factors—intermolecular dynamics involving the C_5H_5-M bond [168,169], change in character of this bond under the influence of strongly solvating solvents [169-172], bridge formation by the cyclopentadienyl ligand [173], maintenance of some form of dynamics in the crystal [174], etc.

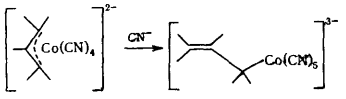
2. $\sigma-\pi$ Transitions

The $\sigma-\pi$ transitions often encountered in organometallic chemistry are investigated by various physicochemical methods, including nuclear magnetic resonance (available information on this topic has been reviewed [175]). $\sigma\pi$-Reactions are usually intermolecular. Thus n.m.r. observations have been reported on irreversible



(11)

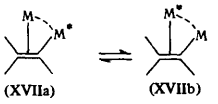
and reversible $\sigma-\pi$ transformations in ethylenic complexes of platinum [176,177]. Papers have appeared on irreversible and reversible $\sigma-\pi$ transitions in π-allylic complexes [178-181], in particular on the reversible reaction



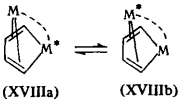
(12)

investigated by n.m.r. [182,183] (such transitions in π-allylic complexes gave rise to a lively controversy—see reviews [5,94] and subsequent communications [184,185]).

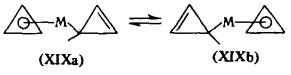
However, there are very few examples of $\sigma-\pi$ transitions that are actually intramolecular. Change in the valency state of the metal in the direction of the given ligand (change in the "connectedness" of the metal–ligand fragment) in compounds possessing stereochemical nonrigidity of this type should, of course, be balanced by the "internal resources" of the molecule. This condition can be realised (at least for degenerate $\sigma-\pi$ transitions) by e.g. combining in one molecule two formally identical metal–ligand fragments, two metals attached to a single ligand by different bonds (structures XVII and XVIII), or two ligands attached in different ways to one metal (structures XIX–XXI):



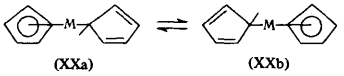
(XVIIa) (XVIIb) (13)



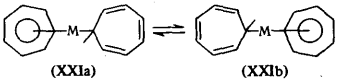
(XVIIIa) (XVIIIb) (14)



(XIXa) (XIXb) (15)



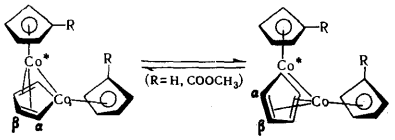
(XXa) (XXb) (16)



(XXIa) (XXIb) (17)

The two metals or ligands may be either structurally isolated or have some additional bond to form a kind of "cluster". Under appropriate temperature conditions the metal–ligand fragments may be expected to interchange functions, and the rates of certain of these degenerate processes may lie in a range suitable for n.m.r. observation.

Examples are known of dimetal compounds of type (XVII), [186-190] but there are at present no reports of the observation of degenerate $\sigma-\pi$ reactions (13) in them. Among dimetal complexes (XVIII) [191,192] "dynamic" derivatives—the dicobalt compounds (XXII: R = H, $COOCH_3$)—are known [193,194]. In these compounds one metal atom is attached to the butadiene fragment by two metal–carbon σ-bonds, and the other by a π-C_4H_4-M π-bond. The two π-cyclopentadienyl ligands are then situated in different environments, and are therefore diastereotopic. Dynamic n.m.r. investigation of solutions of (XXII) indicates that the indicator groups (π-C_5H_5 and CH_3 respectively with R = H and $COOCH_3$) are anisochronous at room temperature, but become isochronous at higher temperatures. However, shielding of the diastereotopic α- and β-diene protons is maintained when dynamic equivalence of the indicator groups appears in the high-temperature spectra. These temperature changes correspond most probably to intramolecular reactions (18) (their rates are independent of concentration), in which each metal atom occupies alternately one of two nonequivalent positions—that in which it forms a π-butadiene bond or the position in which it is attached to the ends of the butadiene fragment by two σ-bonds:



(XXIIa) (XXIIb) (18)

Degenerate $\sigma-\pi$ transitions (15)–(17) are possible between the rings in compounds having $M(\pi\text{-}C_nH_n)(\sigma\text{-}C_nH_n)$ as principal fragment. Processes (15) and (17) for $n = 3$ and 7 respectively have not yet been investigated. With $n = 5$ process (16) has been observed in the n.m.r. examination of the compounds $(C_5H_5)_4M$, $(C_5H_5)_3MX$, $(C_5H_5)_2MXY$, etc. [150,151,154,155,160-163], and can be expected over a wider range of structures. In particular, the low-temperature n.m.r. spectra of certain $(C_5H_5)_4M$ derivatives [160-163] and $(C_5H_5)_3MoNO$, [150,151] together with X-ray examination of crystalline specimens [157,158,161,195,196], show that a C_5H_5-M bond occurs in two forms—delocalised π-bond (spectrum A_5) and localised M–C σ-bond (spectrum AA'BB'X)—within the same molecule. At higher temperatures the set of signals corresponding to the σ-C_5H_5 group degenerates into a single A_5 signal, so that two singlets can be observed, corresponding respectively to protons of the π-C_5H_5 group and the averaged signal due to protons of the σ-C_5H_5 group. At still higher temperatures further changes are observed in the spectrum, accompanied by coalescence of the two signals into one. Thus not only endocyclic $\sigma-\sigma$ transitions (10) take place in these compounds but also $\sigma-\pi$ conversions (16), in which the metal is attached to each cyclopentadienyl ligand alternately by a σ-bond and by a π-bond.

3. $\pi-\pi$ Transitions

Dynamic n.m.r. spectral study of $\pi-\pi$ transitions—dynamic processes of a fundamentally novel type for chemistry—began only during 1966–1967. However, the

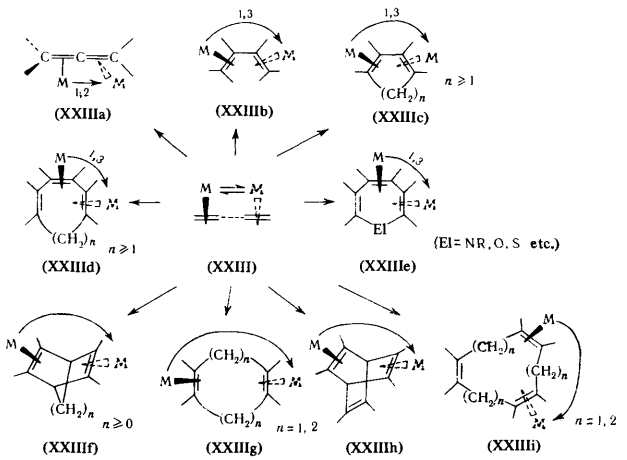
number of known examples is already fairly large, and research is extending to ever new classes of organometallic compounds.

(*a*) $\pi-\pi$ Transitions in derivatives with a ligand having an open system of π-electrons

Schemes 5 and 6 show several types of complexes in which $\pi-\pi$ migration of one metal-containing group is theoretically possible with maintenance of the "connectedness" of the π-metal–ligand fragment in the ground state. The main feature of these structures is the open chain of π-electrons in the carbon skeleton of the ligand.

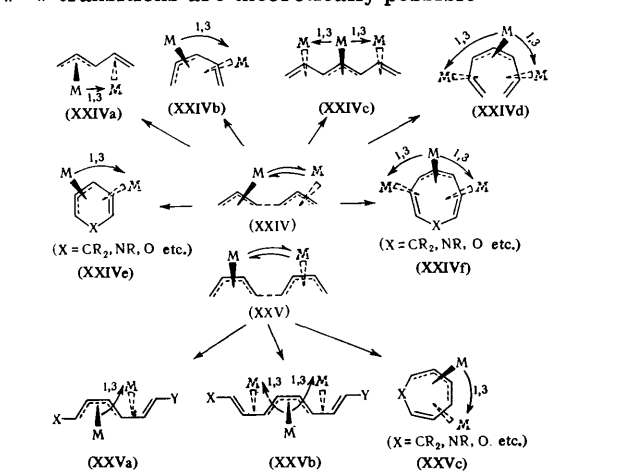
Scheme 5

Some types of ethylenic π-complexes in systems in which the ligand has an open chain of π-electrons and in which $\pi-\pi$ transitions are theoretically possible



Scheme 6

Some types of π-allylic and π-butadiene complexes in systems with an open chain of π-electrons, in which $\pi-\pi$ transitions are theoretically possible

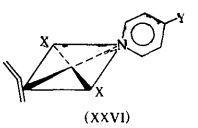


As a consequence, movements of the metal-containing group directed to one side along the perimeter of the unsaturated chain are excluded, and only "vibrational" transitions (degenerate or non-degenerate) between two or more centres are possible. The selection of systems assembled in Schemes 5 and 6 is obviously in considerable measure formal, so that each requires special examination of the conditions under which transitions can actually occur. 1,2-Transitions, involving migration of the metal-containing group to an adjacent C–C bond, are obviously possible only in a limited number of systems. The 1,3- and 1,4-types of migration, as well as more complicated transitions, are formally possible in a wider range of systems. It must be noted that not all the types of organometallic compounds in Schemes 5 and 6 are known at present. Even among those structures which have already been prepared [192,197–200], however, metallotropic $\pi-\pi$ transitions have been investigated so far in isolated cases.

The first investigation of metallotropic $\pi-\pi$ transitions in π-complexes having an open system of π-electrons was made by Ben-Shoshan and Pettit [201] on an allene derivative of iron (structure XXIIIa). In compounds of this type the metal is coordinated with only one multiple bond of the ligand [201–206]. Dynamic n.m.r. investigations have since been extended to compounds of other metals [204,205].

At sufficiently low temperatures the proton n.m.r. spectra of the tetramethylallene complexes π-$C_7H_{12}Fe(CO)_4$ and π-$C_7H_{12}PtCl_2py$ contain three singlet signals corresponding to the "frozen" structure of the compounds—two non-equivalent non-coordinated methyl groups and two equivalent coordinated groups—of relative intensities 1 : 1 : 2. With rise in temperature all the signals coalesce into a single signal, the effect being unaffected by the addition of free tetramethylallene and pyridine to the solution (at temperatures not exceeding $-40°C$). In the spectrum of $(\pi$-$C_7H_{12}PtCl_2)_2$, a compound of lower symmetry, four methyl singlets of equal intensity are observed at $-70°C$, which merge into one signal when the solution warms up to room temperature. Here $^{195}Pt-{}^1H$ spin–spin interaction is observed throughout the temperature range. The effect is independent of the concentration of the complex and of the addition of free tetramethylallene or another tetramethylallene complex [201,204,205].

These experimental facts are explained by intramolecular $\pi-\pi$ 1,2-transitions of the metal atom from one double bond to the other (XXIIIa). [201] The rate of migration of the metal depends significantly on the structure of the complex. Thus it varies appreciably in the compounds

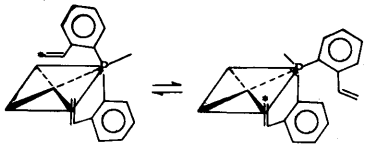


(where X = Cl and M = Pt) on such slight perturbations as changing the substituent Y. [204] The effect is still more striking with more profound structural changes: whereas the process is observed in the spectrum of tetramethylallene derivatives of iron and platinum, it has not yet been detected in allene and 1,1-dimethylallene derivatives of platinum, nor in the allene complex of nickel and the tetramethylallene complex of rhodium [201–206].

Investigation of the dynamic behaviour of other ethylenic π-complexes shown in Scheme 5 and also of other analogous systems awaits our research workers. We will mention certain specific types of $\pi-\pi$ migration studied in ethylenic complexes. Thus the dynamic behaviour of the compound

$Co(\pi\text{-}C_8H_8)\pi\text{-}C_5H_5$, in which the cyclo-octatetraene ligand has 1,5-attachment to the cobalt atom, has been examined[27]. Rise in temperature produces reversible spectral changes, confirming the occurrence of a $\pi-\pi$ transition in the system.

A peculiar example of a $\pi-\pi$ transition in an ethylenic system has been established[207] in an investigation of the proton n.m.r. spectra of tri-*o*-styrylphosphineplatinum and the corresponding arsine and stibine complexes. These compounds obviously have a square planar structure. A single ABX set of signals, corresponding to the two types of ethylenic groups—both uncomplexed and coordinated with the platinum atom—is observed in their n.m.r. spectra at room temperature. Signs of complex formation (displacement of the ethylenic signals towards higher fields relative to the initial ligands and decrease in the proton–proton interaction constants J_{cis} and J_{trans}) are appreciably less marked than in other known π-ethylenic derivatives of platinum[208-211]. The splitting constant $J_{^{195}Pt-^{1}H}$ with one of the protons in the given phosphine complex is about one-third of its value in the usual π-ethylenic complexes of bivalent platinum[208-211]. All these spectral peculiarities are consistent with quite rapid $\pi-\pi$ transitions



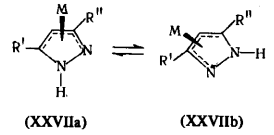
(19)

as a result of which all the spectral characteristics of coordinated and uncoordinated double bonds are averaged out. The process is assumed to be intramolecular with a five-coordinated transition stage.

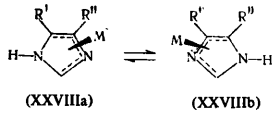
Papers on migration in π-allylic systems (XXIV) have not yet appeared, whereas corresponding n.m.r. data are already known for several π-butadiene structures (XXV). It is found in particular that, in the open systems (XXVa) and (XXVb), $\pi-\pi$ transitions between isomers having somewhat different properties (X ≠ Y) are slow on the n.m.r. time scale. Because of the non-equilibrium character of the process, the n.m.r. recording of such transitions involves merely analytical measurement of the ratio of the isomers. The path of migration of the group M = $Fe(CO)_3$ in compounds (XXVa) and (XXVb) is more or less obvious: only 1,3-transitions, which require no rearrangement of the system of valency bonds, are possible. The "connectedness" of the fragment is assumed to diminish in the transition state, with formation of a π-ethylenic structure ($h^4 \rightarrow [h^2] \rightarrow h^4$).[212-214]

A unique route for intermolecular transformations—$\pi-\pi$ 1,3-transfers of the metal-containing group from one diene fragment to another—is possible also in carbocyclic and heterocyclic compounds (XXVc) having an acyclic system of multiple bonds. Among compounds (XXVc) that have been studied by n.m.r.,[192,200] however, this dynamics has hitherto been observed only in derivatives having X = NR.[215,216] At 0°C the spectrum of the ethylenic portion of the ^{1}H-azepine derivative corresponds to the instantaneous structure in which the tricarbonyliron group is coordinated with only one diene fragment; at room temperature the signals become blurred; and at 65–85°C the spectrum degenerates into a spin system corresponding to dynamic equivalence of the two diene fragments. These spectral changes were interpreted as evidence of the speeding up of transfers of the group M = $Fe(CO)_3$ between two structurally possible positions (another type of dynamics—acceleration of rotation about the N–R bond—is also possible, and appropriate spectral changes have been attributed to it; inversion of the nitrogen atom in this compound is probably quite rapid).

Tricarbonyliron derivatives of pyrazole and imidazole have been prepared[217], and most probably have a π-butadiene structure (XXVII and XXVIII). Their d.n.m.r. investigation showed significant differences between high- and low-temperature spectra: whereas at sufficiently low temperatures the indicator groups R′ and R″ (CH_3 or H) are anisochronous and hence diastereotopic, they become isochronous as the temperature gradually rises. The observed spectral changes might be explained by acceleration of the $\pi-\pi$ transitions a ⇌ b (1,2-transitions for the pyrazole derivatives (XXVII), and 1,3-transitions for the imidazole derivatives (XXVIII); a "counter" rearrangement of the system of double bonds is assumed in both cases) associated with intermolecular and/or intramolecular $\sigma-\sigma$ migration of NH protons:



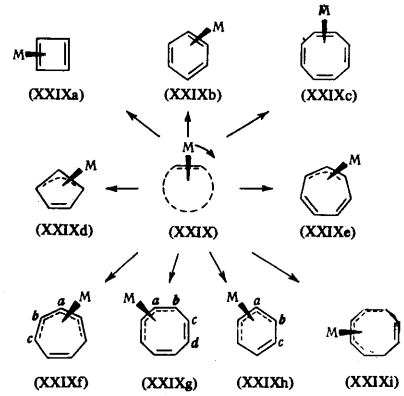
(XXVIIa) (XXVIIb) (20)



(XXVIIIa) (XXVIIIb) (21)

Scheme 7

Some types of compounds with a cyclic system of π-electrons in the ligand, where $\pi-\pi$ transitions are possible



(XXIXa) (XXIXb) (XXIXc) (XXIXd) (XXIX) (XXIXe) (XXIXf) (XXIXg) (XXIXh) (XXIXi)

(*b*) $\pi-\pi$ Transitions in systems with a ligand having a closed chain of π-electrons

Scheme 7 assembles several types of organometallic π-complexes in which a carbocyclic ligand has a cyclic system of π-electrons. The transition metal, because of its "electronic requirements", is unable to coordinate with all the π-electrons simultaneously, but only with an individual segment of the carbon ring. In contrast to the

derivatives discussed in the preceding subsection, the complexes (XXIX) may in principle possess more intense and varied $\pi-\pi$ dynamics: not only "vibrational" but also unidirectional translational movements of metal-containing groups are possible in them; and the π-bond in the transition state of complexex (XXIX) can assume the energetically unforbidden form (I), which is formally similar to the structure of the ground state in many π-complexes. However, these features of the derivatives (XXIX) complicate substantially discussion of the mechanisms of their $\pi-\pi$ transformations because of the multiplicity of the latter.

Among the mono-olefinic π-complexes (XXIXa–c) $\pi-\pi$ transitions have so far been detected in the platinum derivative (XXIXb). The process is intramolecular, since spin–spin interaction between platinum-195 and the ring nuclei is observed throughout the temperature range. The n.m.r. spectrum of the compound in the "frozen" state is consistent with X-ray data [218].

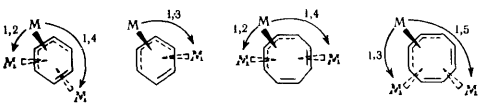
Information is available on the π-allylic complexes (XXIXd, e). The complex (XXIXd) has been prepared [219], and an aluminium derivative of this type has been studied by gas-phase electron diffraction [220]. Cycloheptatrienyl complexes of molybdenum, tungsten, cobalt, and iron of the type (XXIXe) have been described [19,221–229], and their stereochemical non-rigidity has been investigated by d.n.m.r. on several examples. Unfortunately, the structure (XXIXe) (based on the "electronic requirements" of the metal taking into account its bonds in the rest of the complex) is not uniquely possible. Low-temperature n.m.r. investigations of these complexes indicate the possibility not of a π-allylic but of a C_7H_7-M σ-bond [94,224], although in the fairly specific pyrazolylborate derivative of molybdenum the bond in the crystal is actually π-allylic [226]. Thus a more exact discussion of the mechanism of metallotropic transitions in the complexes (XXIXe) ($\pi-\pi$, $\sigma-\sigma$, or more complicated) will evidently be possible only after their "instantaneous" structure has been elucidated both in solution and in the crystal.

The preparation and the n.m.r. investigation of the derivatives $[C_7H_7Fe(CO)_3]^+$ and $C_7H_7Mn(CO)_3$ have been reported [16,219]. The low-temperature limiting spectrum of these compounds corresponds to the "frozen" structure (XXIXf) with anisochronous protons of the diastereotopic groups $a-d$. Degeneration of the spectrum into A_7 at higher temperatures indicates that the ligand nuclei become dynamically equivalent. The observed spectral changes are due to acceleration of $\pi-\pi$ transitions of the metal-containing group, but insufficient data are yet available for assessment of the more detailed mechanism of these transitions.

The largest number of papers are concerned with $\pi-\pi$ transitions in butadiene π-complexes (XXIXh) and (XXIXg), and much of the information on their dynamic behaviour has been obtained only during most recent years. The protons of the diastereotopic indicator groups ($a-d$ in XXIXg, and $a-c$ in XXIXh) are anisochronous at sufficiently low temperatures, but become isochronous at higher temperatures. The temperature dependence of the line form has been investigated experimentally, and the theoretical form of the line has been calculated for various lifetimes of the molecules in the "frozen" state.

The history of the d.n.m.r. study of the cyclo-octatetraene derivatives (XXIXg) is extremely dramatic. Originally it was known only that the protons of the cyclo-octatetraene ligand were isochronous in solutions of $\pi-C_8H_8Fe(CO)_3$ and similar compounds: the proton n.m.r. spectrum contained a narrow singlet independently of the choice of solvent or of solution temperature right down to $-60°C$. [230–232] As a result it was suggested that this ligand has a planar structure and that all its eight protons are equivalent (structure I: $n = 8$). [230,231,233] However, this hypothesis was not confirmed by a structural examination of $\pi-C_8H_8M(CO)_3$ molecules (M = Fe, [13] Ru [234]). Dickens and Lipscomb [13] found that, at least in the crystal, the $M(CO)_3$ group forms a π-bond with only one conjugated diene unit (structure XXIXg). These workers suggested that the equivalence of the protons of the $\pi-C_8H_8-M$ bond in a solution of the iron complex, in contrast to the crystal, was for the n.m.r. observer not static but dynamic in origin, and resulted from the rapid movement of the metal-containing group between several possible 1,3-diene positions. During 1966–1967 several groups of workers were able to reach sufficiently low temperatures to "freeze" the n.m.r. spectral pattern for both complexes and several related compounds [23,25,26,235–239]. The instantaneous structure of these compounds in solution was actually found to be identical with their structure in the crystal: as the temperature fell the spectrum of the π-cyclo-octatetraene ligand revealed four anisochronous indicator groups, corresponding to four types of diastereotopic nuclei in the ligand. Similar results have since been obtained in investigations of these and analogous derivatives of type (XXIXg) (M = Fe, Ru, Os) by proton [240–244] and carbon-13 [245] nuclear magnetic resonance. Evidence has also been obtained in support of the intramolecular character of the observed dynamics. For example, study of a solution of a mixture of cyclo-octatetraene and the complex $\pi-C_8H_8Fe(CO)_3$ at room temperature revealed no interaction between them: the ring protons of both compounds were anisochronous in the n.m.r. spectrum [231]. Finally, it has been found [246,247] that in these and related compounds $\pi-\pi$ dynamics is maintained even in the crystal. Only lowering the temperature of the crystal led to an (apparent) arrest of the process, i.e. to a decrease in the frequency of transitions to around 1 kHz (limit of sensitivity of the method employed).

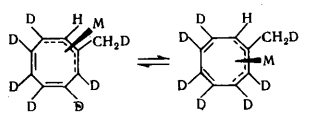
Consideration of the detailed mechanism of $\pi-\pi$ processes in π-cyclo-octatetraene derivatives (XXIXg) involves a choice [244] between several possibilities—1,2-, 1,3-, 1,4-, or 1,5-transitions (structures XXXc and XXXd)—with formation of a non-planar transition state or a $\pi-\pi$ transition via a planar transition state (I: $n = 8$) with a statistical distribution of products. Analogous mechanisms (XXXa, b) are suggested for the derivatives (XXIXh). [248] With 1,2- and 1,4-transitions (XXXa, c), of course, spatial displacement of the metal (if it occurs at all) must be accompanied by redistribution of the system of multiple bonds in the ligand (valency tautomerism), but with 1,3- and 1,5-transitions (XXXb, d) the bond system will be unchanged:



(XXXa) (XXXb) (XXXc) (XXXd)

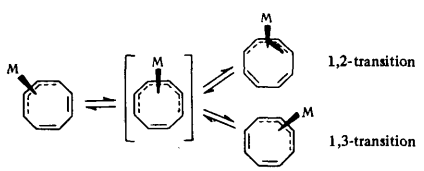
The experimental results are discussed on the basis of these possible mechanisms. Thus comparison of experimental and theoretical n.m.r. line forms indicates [244] that, in derivatives (XXIXg) of metals of the iron subgroup, both experimental and theoretical patterns are least consistent with 1,4- and 1,5-transitions, and also with the statistical mechanism involving the transition state (I: $n = 8$). The temperature dependence of the spectrum of $\pi-C_8H_8Ru(CO)_3$ led to the conclusion [237] that $\pi-\pi$ transitions

in systems such as (XXIXg) are effected by successive 1,2-shifts of the metal-containing group, and that a mechanism involving $\pi-\pi$ 1,3-transitions is unacceptable. A similar conclusion has been reached for compounds of type (XXIXh).[248] This is consistent with Anet's experimental results on the compound (XXXI),[236] which may in principle exist as very many structures, although contributions by structures other than (XXXIa, b) to the high-temperature spectrum are extremely small. Only two equivalent structures—(XXXIa) and (XXXIb)—are observed in the low-temperature boundary spectrum. Thus the intramolecular dynamics in this compound reduces to degenerate $\pi-\pi$ 1,2-transitions:



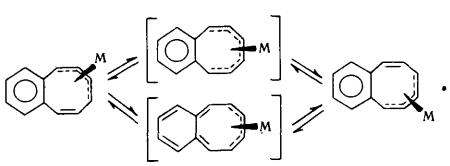
(XXXIa) (XXXIb) (22)

However, conclusions on 1,2-migration have since become somewhat less categorical. Thus the theoretical pattern of migration of the metal in π-$C_8H_8Ru(CO)_3$ agrees best with experiment only on the assumption of definite contamination of 1,2-transitions by a 1,3-type of mechanism[244]. On the other hand, study of the temperature dependence of the spectrum of π-$C_8H_8Os(CO)_3$ reveals several additional difficulties connected with the complexity of obtaining the theoretical n.m.r. line form for such multispin systems[243]:

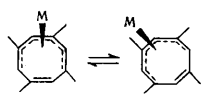


(23)

It is probable that $\pi-\pi$ transitions in the derivatives (XXIXg) and (XXIXh) can be accomplished both by one of the suggested mechanisms (1,2-, 1,3-, 1,4-, and 1,5-transitions or the statistical mechanism) and by some other mechanism. For cyclo-octatetraene derivatives, in particular, mechanism (23) can be suggested as a hypothesis. Vibrations of the ring in the transition state would then be accompanied by an increase in the "connectedness" of the metal ($h^4 \rightarrow [h^6] \rightarrow h^4$), which allows for the objective result[244] that each step in the reaction involves formation of a mixture of 1,2- and 1,3-transition products. A mechanism with intermediate increase in the "connectedness" of the metal—as an alternative to a mechanism involving intermediate formation of a quinoid structure[249]—is useful in considering $\pi-\pi$ transitions of the tricarbonyliron group in benzo- and naphtho-cyclo-octatetraenes:



Stereochemical non-rigidity has been investigated[23,24,222,240,241,250,251] in the cyclo-octatetraene derivatives (XXIXi) of metals of the chromium and iron subgroups. However, the difficulties of interpreting the low-temperature boundary spectrum prevented sufficiently detailed information from being obtained on the mechanism of dynamics in the cyclo-octatetraene derivatives themselves[23,222]. These difficulties were overcome to a certain extent by using 1,3,5,7-tetramethylcyclo-octatetraene as ligand[24,251]. Over the range adjacent to the temperature at which the low-temperature boundary spectrum is observed the process is effected by 1,2-transitions:

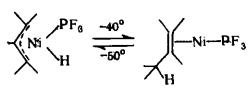


(24)

However, the spectral changes observed on further heating indicate that the process becomes more complicated. Under these conditions the stereochemical non-rigidity is probably due also to the formation in the transition state of the planar structure (I) with enhancement of "connectedness" ($h^6 \rightarrow [h^8] \rightarrow h^6$).

(*c*) $\pi-\pi$ Transitions accompanied by change in the "connectedness" of the metal in the metal–ligand fragment

Little study has yet been made of $\pi-\pi$ transitions of this type. An illustration is the reversible reaction

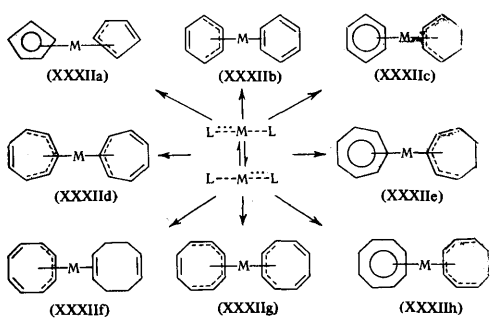


(25)

which has been investigated by n.m.r.[252] However, this reaction involves a $\sigma-\sigma$ transfer of a proton as well as a $\pi-\pi$ transfer of the metal, so that the composition of the metal–ligand fragment itself changes.

Scheme 8

Some types of π-complexes containing a $(\pi$-$C_nH_n)_2M$ fragment in which intercyclic $\pi-\pi$ transitions are fundamentally possible



(XXXIIa) (XXXIIb) (XXXIIc) (XXXIId) (XXXIIe) (XXXIIf) (XXXIIg) (XXXIIh)

A "purer" case of these processes is provided by degenerate intramolecular transitions of like ligands between non-equivalent states. Several types of complexes having $(\pi$-$C_nH_n)_2M$ as the main fragment are assembled systematically in Scheme 8. Dynamics of this kind can in principle occur in such compounds, provided that the variation in "connectedness" of each metal–ligand unit is produced by the "internal resources" of the other unit. Intercyclic $\pi-\pi$ exchanges are not yet known for rings containing an odd number of carbon atoms. Only one of the possible types of these reactions has been

investigated by n.m.r. for each of the "even" rings. Such reactions can in principle occur both in dicyclic compounds $(\pi\text{-}C_nH_n)_2M$ not containing any other ligands and in more complicated compounds—$(\pi\text{-}C_nH_n)_2MR$, $(\pi\text{-}C_nH_n)_2.MCO$, $(\pi\text{-}C_nH_n)_2MNO$, $(\pi\text{-}C_nH_n)_2M(CO)_2$, etc.

Structural data [253] indicate that one ring in the compound $(\pi\text{-}C_8H_8)_2Fe$ forms a diene π-bond, and the other a triene π-bond (structure XXXIIg). A d.n.m.r. investigation [240] suggests that, at temperatures below $-84°C$, the metal undergoes vigorous migration in the "diene" ring (all its protons are isochronous) and is "frozen" with respect to the triene ring (four types of protons are anisochronous). At higher temperatures the metal migrates rapidly inside both cyclo-octatetraene ligands—diene and triene (the protons in each of them become isochronous)— and above $-35°C$ the averaged signals due to the two rings coalesce into one. Thus cyclo-octatetraene ligands attached to an iron atom by unequal π-bonds exchange the types of bonds quite rapidly and entirely synchronously.

Similar conclusions follow from d.n.m.r. data on the ruthenium complex (XXXIIc). Two types of bonds—π-diene and π-arene—are present in the crystal [254]. Nevertheless, the temperature dependence of the n.m.r. spectrum of this complex reveals changes indicating the occurrence of quite rapid intercyclic $\pi-\pi$ transitions [255]. Finally, yet another type of dynamics, not shown in Scheme 8, has been observed in $(C_8H_8)_2M$ derivatives [256].

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Institute of Organoelementary Compounds, USSR Academy of Sciences, Moscow

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Molecular Complexes in the Liquid-phase Halogenation of Unsaturated Compounds

G.B.Sergeev, Yu.A.Serguchev, and V.V.Smirnov

Results on the halogenation of unsaturated compounds in the liquid phase are discussed. The possibility is examined that molecular complexes are involved in the polar, molecular, and radical mechanisms of addition. A list of 151 references is included.

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I. INTRODUCTION

Reactions involving the addition of halogens at a multiple bond are important because of their wide distribution and their practical value. The electrophilic addition of halogens at a double bond was surveyed in a monograph[1]. A large amount of factual information has accumulated in recent years, and has been interpreted mainly on the basis of an ionic mechanism. Nevertheless, the existence of halogen–alkene molecular complexes and of complexes of halogens with several compounds used as solvents has been demonstrated experimentally. The role of such complexes in the mechanism of the halogenation of multiple bonds has not been finally established.

The Review analyses, mainly from an energetic point of view, the possibility that complexes are involved in polar, molecular, and radical mechanisms of the liquid-phase halogenation of unsaturated compounds.

The view that carbonium ions of varied structures were reaction intermediates was based on the work of Francis[2] and Roberts and Kimball[3]. The importance of the role of donor–acceptor interactions in reaction mechanisms was noted by Shilov[4,5]. Dewar developed the concept of π-complexes[6]. The theory of charge-transfer complexes was formulated by Mulliken[7].

The structure, physicochemical properties, and methods of studying molecular complexes in systems in which no appreciable chemical reaction is occurring have been

discussed in monographs [8-10]. The formation of halogen–alkene complexes is accompanied by a chemical change in the components, and therefore is especially interesting. The role of molecular complexes in the halogenation of unsaturated compounds has been partly considered in reviews [5,11-13].

II. MOLECULAR COMPLEXES OF HALOGENS WITH ALKENES

Molecular complexes of halogens with alkenes have been investigated mainly spectrophotometrically [14-18]. Charge-transfer bands appear in the spectra when halogens (acceptors) interact with alkenes (donors). The complexes absorb in the range 240–320 nm in the ultraviolet. The charge-transfer band $h\nu$ is related to the ionisation potential I_V of the alkenes by the equations [15] $h\nu(Br_2) = 0.69I_V - 2.09$ and $h\nu(Cl_2) = 0.51I_V + 0.03$.

Table 1. Enthalpies ΔH and equilibrium constants K_C of alkene–halogen complexes in non-polar solvents.

Alkene	I_2		Ref.	Br_2		Ref.	Cl_2		Ref.
	$-\Delta H$, kcal mole^{-1}	$K_C^{298°}$, M^{-1}		$-\Delta H$, kcal mole^{-1}	$K_C^{298°}$, M^{-1}		$-\Delta H$, kcal mole^{-1}	$K_C^{298°}$, M^{-1}	
Hex-1-ene	2.8	0.20	19	3.3	0.145	19	1.7	0.24	17
Cyclohexene	2.3	0.52	18	4.0	0.36	16	2.7	0.33	17
4-Methyl-pent-1-ene	3.3	0.24	19	2.8	0.33	19	—	—	
Hept-3-ene	4.0	0.72	19	4.0	—	19	—	—	
Cyclopentene	2.8	0.43	18	—	—		—	—	
Styrene	2.1		20	—	—		—	—	
trans-Stilbene	1.8	—	20	—	—		—	—	
	2.6								

Inadequate study has been made of the complexes of halogens with alkenes, owing to the experimental difficulties involved in investigations in the reacting systems. Table 1 summarises experimental results on the thermodynamic functions of the complexes of reactive alkenes with halogens. Data have been published also on the complexes of cyclohexene with iodine bromide ($\Delta H = -7.5$ kcal mole^{-1} and $K_C^{298°} = 2.2$ M^{-1}) [16] and of hex-1-ene with iodine chloride (-1.5 kcal mole^{-1} and 2.0 M^{-1}) [19].

Table 1 shows that halogens form weak complexes with alkenes, characterised by low equilibrium constants ($K_C < 1$) and enthalpies of formation ($|\Delta H| < 5$ kcal mole^{-1}). The latter values are comparable with the activation energies of many halogenations of alkenes, and may make an appreciable contribution to the energetics of the process.

Table 2 lists data on the structural and physicochemical properties of the halogens.

Scheme 1 shows the mechanism of the reaction of halogens with alkenes [12]. Initially an internal ion-pair, analogous to Dewar's π-complexes [6] or to σ-complexes in aromatic substitution [23], is formed from a labile halogen–alkene π-complex or directly from the original molecules. This complex then rearranges into the reaction products or else breaks down into solvated ions, whose interaction results in formation of the product. In the termolecular reactions characteristic of the addition of bromine and iodine the anion X^- is replaced by X_3^-. The rate of the reaction is governed by the passage of the system through the transition states (II) (ionisation) and (IV) (separation or migration of the ions in the ion-pair).

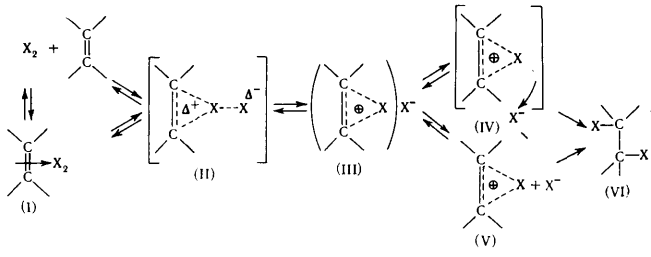
Let us examine the rôle of halogen–alkene complexes (I) in formation of the transition state (II) under conditions such that the contribution by solvation effects can be neglected. This transition state (II) may be established both by collision of activated X_2 molecules with the unsaturated compound and by charge redistribution in the molecular complex (I). The latter follows from a comparison of structures (I) and (II).

Table 2. Some physicochemical properties of halogens [21,22].

Mol.	Internuclear distance, Å	Anionic radius, Å	Dissociation energy at 298°K, kcal mole^{-1}	Electron affinity	
				mol., eV	atom, eV
I_2	2.667	2.20	36.1	2.4	3.29
Br_2	2.283	1.81	46.1	2.6	3.54
Cl_2	1.998	1.06	57.9	1.70	3.76
ClI	2.321	—	50.5	—	—
BrI	—	—	42.5	—	—

Changes occur mainly in two distances—from the halogen molecule to the centre of the double bond r_{C-X} and between the nuclei in the halogen—as the molecule approaches the double bond with formation of an ion-pair.

Scheme 1.



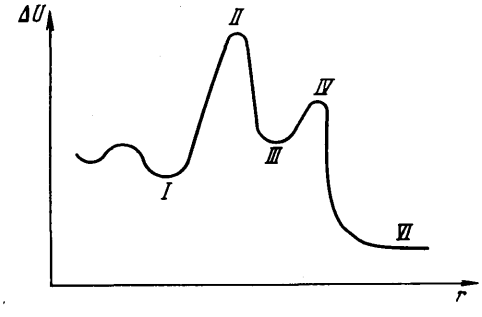


Figure 1. Variation in potential energy along reaction path of heterolytic halogenation.

The former distance r_{C-X} changes from infinity to the halogen–double bond distance in the carbonium ion. The internuclear distance X–X in the bromine molecule, for example, is < 2.3 Å. The X–X distance in the ion-pair can be estimated as the sum of the radii of the negative

ion and of the uncharged atom. For bromine this sum is 3.1 Å, which exceeds the internuclear distance in the molecule by 0.8 Å. Since these distances are the chief variables on formation of an ion-pair, the potential-energy surface of the system can be plotted with r_{C-X} and r_{X-X} as coordinates. The distance r_{C-X} is shorter in the complex than in the initial molecules. X-Ray diffraction has established that the formation of complexes involving halogens leads to some increase in the internuclear distances in the latter molecules[24,25]. Thus

$$(r_{X-X})_{init} < (r_{X-X})_{complex} < (r_{X-X})_{transn.\ state},$$

$$(r_{C-X})_{init} \gg (r_{C-X})_{complex} > (r_{C-X})_{transn.\ state}.$$

Hence the π-complex lies on the reaction path between the initial molecules and the transition state. It can be shown similarly that the σ-complex (internal ion-pair III) also lies on the reaction path between (II) and (IV).

Thus application of the transition-state theory to polar halogenation indicates that halogen-alkene complexes may be involved as intermediate species. Fig. 1 illustrates the variation in the potential energy along the reaction path.

III. POLAR MECHANISM

The energy barriers at individual stages in Scheme 1 can be estimated by means of a model involving electrostatic interactions.

The potential barrier (II) in Scheme 1 is connected with ionisation of the molecular complex. This process is analogous to complete electron transfer from donor to acceptor with energy equal to the difference between the ionisation potential of the donor and the electron affinity of the acceptor. The energy of Coulombic attraction between the oppositely charged ions is gained.

Formation of a bridging halogenonium cation of the type



is accompanied by partial dehybridisation of the double-bonded carbon atoms and the appearance of incompletely covalent C–X bonds. Quantum-mechanical calculation of the relative stabilities of ions differing in structure enables the contribution of these two factors to be estimated[26]. With ethylene, chloronium and bromonium bridges are more stable than the corresponding classical carbonium ions of type



by 28.4 and 26 kcal mole^{-1} respectively. The carbonium ion involves complete rupture of the double bond and formation of a C–X bond, and the heat of reaction can be estimated as the difference between the corresponding energy changes. Adding 28.4 or 26 kcal mole^{-1} to the result yields the stabilisation energy of the ion E_{st} due to formation of new bonds. Depending on the alkene E_{st} = 45–49 and 31–35 kcal mole^{-1} for chlorine and bromine respectively. On the assumption that an iodonium bridge is 20 kcal mole^{-1} more stable than the open system we obtain $E_{st} \simeq 7$–11 kcal mole^{-1}.

Thus the energy of the system during conversion of the π-complex into an ion-pair is described by the formula

$$U = e(I - E_x) - \sum_{ij} \frac{e_i e_j}{r_{ij}} - E_{st} \qquad (1)$$

where I is the ionisation potential of the donor, E_X the electron affinity of the acceptor, r_{ij} the distance between the centres of i and j atoms bearing charges e_i and e_j respectively, $e = \Sigma e_i$ the total transferred charge, and E_{st} the stabilisation energy of the carbonium cation, which depends on the fraction of the charge transferred. Quantum-mechanical calculation of the structures of ethylene–chloronium and ethylene–bromonium cations shows that up to 30–40% of unit positive charge is concentrated on the halogen atom[26,27]. Hence the charge is uniformly distributed among all the vertices of the triangle. Calculations indicate[26] that the radius of the halogen atom in the cation can be regarded as equal to its covalent radius. Formula (1) can be used to estimate the heat of transition of the complex into the ionised state. In the series of complexes of chlorine, bromine, and iodine with ethylene, hex-1-ene, and cyclohexene the iodine–ethylene ion-pair had the largest heat of formation, and chlorine–cyclohexene the smallest (110 and 30 kcal mole^{-1} respectively).

The heat absorbed on complete charge transfer is not necessarily identical with the activation energy. The first term in Eqn. (1) varies linearly with the amount of charge transferred, and the second term is a quadratic function, so that $U(e_i, r_i)$ may reach a maximum even with incomplete charge transfer. This implies that partial transfer of the electronic charge may prove sufficient in the reactive systems, and further charge separation requires no further energy consumption, but occurs readily as a spontaneous process. The degree of charge transfer at which the potential energy reaches a maximum can be estimated by means of Eqn. (1). If we suppose that internuclear distances cease to depend on the degree of ionisation at charge transfers exceeding $0.5e$, we can then find the value of x corresponding to U_{max} from the condition for a maximum $dU/dx = 0$ (where x is the degree of transfer).

Table 3. Activation energies (kcal mole^{-1}) of formation of ion-pairs.

Alkene	Halogen		
	Cl	Br	I
Ethylene	69	73	110
Hex-1-ene	48	50	84
Cyclohexene	39	40	70

Specific values for I, E_X, E_{st}, and r_{ii} yield values for x_{max} from 0.6–0.7 (cyclohexene and hexene with chlorine) to 1.0 (systems containing iodine and ethylene–bromine). From the values of x_{max} we can calculate U_{max}, i.e. the activation energy of formation of ion-pairs. The results listed in Table 3 exceed those obtained on the basis of a four-membered transition state and the postulate that formation of a hemi-ionic pair is sufficient for reaction[28]. The values in Table 3 give the correct sequence of reactivity for the halogens $Cl_2 > Br_2 \gg I_2$,[1] whereas the opposite sequence was obtained in Ref. 28.

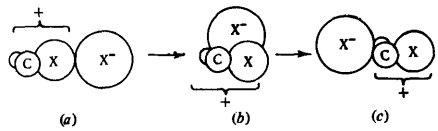
Considering now the probable structure and energetics of the σ-complex, we note that an ion-pair with a linear arrangement of the atoms

$$\overset{\oplus}{>}X....X^-$$

is in a state of unstable equilibrium. Any displacement of

the anion X^- from the plane of the cyclic cation in the direction of the double bond involves a gain in energy. In the stable state of the ion-pair the halide anion is situated above the plane of the carbonium cation, the C–X and X–X distances being minima (Scheme 2).

Scheme 2.



Structure (*b*) is also a σ-complex, the gain in energy on its formation from the unstable ion-pair (*a*) being the depth of the potential well (III) in Fig. 1). To estimate this gain we assume that the radii of atoms and ions in (*a*) and (*b*) are identical. Calculation of the energy of electrostatic attraction in (*b*) shows that (*a*) and (*b*) differ in energy by 38–42 kcal mole^{-1} for all the halogens.

In the last stage of the reaction the anion X^- again passes into the plane of the carbonium cation, but from the side opposite to the second atom (structure *c*). The height of the potential barrier to the transition (*b*) → (*c*) can be estimated as the difference between the Coulombic energies of attraction. Calculation shows it to be small, from 8 to 12 kcal mole^{-1} for iodine and chlorine respectively. Hence it may be expected that the σ-complex will pass readily into the product. The situation is different if this change is impeded, e.g. by steric hindrance. In fact stable complexes, having the character of internal ion-pairs, are formed by the interaction of bromine with sterically hindered alkenes at −78°C [29]. The above estimates show that the limiting step in the reaction is ionisation of the π-complex with formation of an ion-pair (σ-complex).

Table 4. Calculated activation energies (kcal mole^{-1}) in solutions.

Dielectric constant of solvent	Reactants								
	ethylene			hex-1-ene			cyclohexene		
	Cl_2	Br_2	I_2	Cl_2	Br_2	I_2	Cl_2	Br_2	I_2
2.2	39	40	64	28	28	47	22	22	38
4.5	33	35	54	24	25	38	19	20	33
8.0	31	31	51	22	23	36	16	18	30
20.0	28	28	49	18	20	34	15	16	28

1. Effect of Non-specific Solvation on Reaction Velocity

When a polar reaction takes place in a solvent of dielectric constant ε and incapable of specific solvation either of the starting materials or of the transition state, the ion-pair can be regarded as a dipole, and its energy of non-specific solvation can be estimated by means of Kirkwood's formula. We assume that the length of the dipole is the distance between the centre of the anion and the geometric centre in the carbonium cation. The radius of the dipole is the mean of the dimensions of the ion-pair parallel and perpendicular to the axis of the dipole. Solvation energies may reach several tens of kilocalories. Thus the consumption of energy required for ionisation should be appreciably smaller in the liquid phase than in the gas. The potential energy reaches its maximum value with incomplete charge transfer, as in the gas phase. We can find U_{max} by adding in Eqn. (1) a solvation term calculated by means of Kirkwood's formula. The estimated activation energies are given in Table 4.

In sufficiently polar solvents the difference between the activation energies of (*a*) and (*b*) (Scheme 2) plays no appreciable part, and the potential barrier (IV) should not be very high. Traversing the barrier, the reaction system forms the product by continuous passage of the halide anion to the side of the double bond opposite that on which the second X atom is located. Fig. 2 shows the change in the potential-energy profile on passing from the gas phase to a solvent having ε = 8 (for the reaction of chlorine with hex-1-ene). The activation energies for bimolecular polar reactions should be a few tens and 10–20 kcal mole^{-1} in media of low and high dielectric constant respectively.

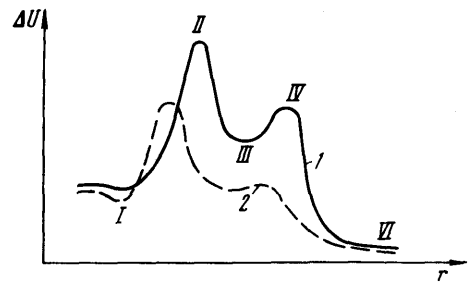


Figure 2. Variation of potential energy along reaction path of hex-1-ene with chlorine in: 1) gas phase; 2) solvent of dielectric constant 8.

The polar character of transition states and intermediate species in halogenation has been confirmed for several alkenes in various solvents by measuring the electrical conductivity during bromination [30]. The conductivity is determined by the degree of charge separation established in the alkene–halogen system. The effect of the solvent varies in parallel with its dielectric constant and its ability to solvate polar and ionic species. Alkenes form a sequence according to their reactivity towards bromination. The conductivity is small in carbon tetrachloride, phenyl bromide, and chloroform, which indicates the absence of ionic states.

The rate of bromination of pent-1-ene has been investigated in water, alcohols, acetic acid, dioxan, Freon, aqueous methanol, and other solvents [31,32]. The second-order rate constant varies widely, from 0.07 to 1.5×10^{-9} M^{-1} min^{-1} in Freon-113 and water respectively. It increases with the dielectric constant of the medium, and is given by the equation $\lg k = 5.40 - 1.164 \lg (k_S/k_0)$, where k_S and k_0 are the solvolysis rate constants for t-butyl chloride at 25°C in the given solvent and in 80% aqueous ethanol respectively.

A qualitative correspondence between the rate constant and the dielectric constant of the medium has been established[33] for the bromination of octene, vinyl acetate, and certain other unsaturated compounds. Direct proportionality of the rate constant to the dielectric constant of the medium was observed also in the chlorination of 3-chloro-1-phenylprop-1-ene in benzene to which more polar solvents had been added[34]. Rates of bromination in a 70:30 methanol–water mixture at 25°C may vary by factors of $\sim 10^4$ depending on the structure of the unsaturated molecule. On passing to methanol itself the rate falls roughly equally for all alkenes, in conformity with the equation $\lg k_{mixt} = 2.6 + 0.9 \lg k_{CH_3OH}$, which suggests that the reaction mechanism remains unchanged[35].

No systematic study has been made of the effect of the dielectric constant of the medium on the activation energy of halogenation. In the bromination of certain aliphatic alkenes in water E_{act} = 8–11 kcal mole^{-1}.[36] The activation energy for the bromination of 1,3-alkenynes in acetic acid varies from 3 to 8.5 kcal mole^{-1}.[37] The bromination of styrene in acetic acid has activation enthalpies of 8–11 kcal mole^{-1} and negative entropies of activation of 27–33 kcal mole^{-1} deg^{-1}.[38] The bimolecular bromination of cinnamic acid in methanol has an activation energy of 9.2 kcal mole^{-1},[39] and 6.1 kcal mole^{-1} is required for the bromination of allyl acetate in acetic acid[40]. The activation energy for the bromination of various alkenes in methanol varies from 7 to 11 kcal mole^{-1}.[41] The activation energies for the chlorination of allyltrimethylammonium perchlorate and 2,3-dichloropropene in acetic acid are 7.4 and 11.2 kcal mole^{-1} respectively[42].

Thus activation energies in polar media vary in the range 5–15 kcal mole^{-1}. This corresponds to the above estimates for a polar mechanism with the rate constant depending on the polarity of the medium.

The ionisation potential is a component of the activation energy and, according to the reaction mechanism assumed (Scheme 1), determines the reactivity of the alkene in the polar medium. A linear dependence of the logarithm of the rate constant on the ionisation potential may be expected in polar media.

2. Dependence of Reaction Velocity on Structure of Alkene

The dependence of the rate of bromination on the structure of the alkene is summarised in the form of correlation equations. Those containing the Taft σ^* [43] and Brown σ^+ [44] parameters are of the form (Table 5)

$$\lg k = \rho \sum \sigma + \text{const}. \qquad (2)$$

A term proportional to the sum of the steric parameters ΣE_S is sometimes detached from the constant in Eqn. (2)[46,47].

Table 5 shows that the parameters ρ have negative values typical of electrophilic reactions. These yield certain conclusions as to the structure of the transition state. Large negative values of ρ probably indicate considerable separation of charges in the transition state with polar solvents. The rate of bromination of tetrasubstituted alkenes correlates with the sum of the Taft σ^* parameters. This suggests that the positive charge in the transition state is uniformly distributed between the two carbon atoms, so that bromination of these compounds involves an intermediate structure of the bridged cation type[46]. As the agent becomes less electrophilic, e.g. on passing from Br_2 to Br_3^-, the value of ρ decreases. The corresponding values for the bromination of substituted stilbenes in acetic acid are −4.21 and −2.02.[52] Correlation equations for chlorination have been obtained only in Ref. 54.

Correlation equations have been published also linking the reaction velocity with parameters other than σ. A linear relation has been found between Γ, representing the electrostatic energy of the halogen–alkene complex in the excited state, and the rate constant for bromination in water: $\Gamma = b + a \lg k_2$.[15] The parameter Γ in turn correlates with the ionisation potential of the alkene: e.g. for bromine complexes $\Gamma = 0.31 I_V + b'$.

Table 5. Correlation equations for liquid-phase polar halogenations.

Alkenes	Halogenating agent	Solvent	Equation	Ref.
RCH = CHR′R″ (R, R′, R″ = alk)	Br_2	MeOH	$\lg k = -5.299\,\Sigma\sigma^* + 0.914\,\Sigma E_s + 7.414$	45
RR′C=CR″R‴ (R, R′, R″, R‴ — Alk)	Br_2	MeOH	$\lg k = -5.221\,\Sigma\sigma^* + 0.896\,\Sigma E_s + 7.381$	46
$CH_2 = CH - CH_2X$ (x = Alk, OH^-, Ph, Cl)	Br_2	MeOH	$\lg k = -3.10\,\Sigma\sigma^* + 8.8$	47
$CH_2 = CH - CHXX'$ (X,X′ = Alk)	Br_2	MeOH	$\lg k = -2.99\,\Sigma\sigma^* + 7.61$	48
(X,X′ — CH_2OH, CH_2Cl, CH_2OEt)	Br_2	0.2 M NaBr	$\lg k = -2.4\,\Sigma\sigma^* + \text{const}$	50
$X - C_6H_4 - CH = CH_2$ (X = Various solvents)	Br_2	ditto	$\lg k = -4.3\,\Sigma\sigma^* + \text{const}$	49
(X = Hal, NO_2)	Br_2	MeCOOH	$\lg k = -4.71\,\Sigma\sigma^* + \text{const}$	53
(X = Hal, NO_2)	Br_2	MeCOOH	$\lg k = -4.21\,\Sigma\sigma^* + \text{const}$	52
(X = Hal, NO_2)	Br_3^-	MeCOOH	$\lg k = -2.02\,\Sigma\sigma^* + \text{const}$	52
$R - C_6H_4 - CH = CH - Ph$ (R = Acceptor)	Br_2	MeOH 0.2 M NaBr	$\lg k = -1.53\,\Sigma\sigma^+ + \text{const}$	51
(R = Donor)	Br_2	ditto	$\lg k = -5.05\,\Sigma\sigma^+ + \text{const}$	51
$CH_2 = CH - C \equiv C - R$ (R = Alk)	Br_2	MeCOOH	$\lg k = -1.35\,\Sigma\sigma^* + \text{const}$	37
$X - C_6H_4 - C \equiv CH$	Br_2	MeCOOH	$\lg k = -5.17\,\Sigma\sigma^+ + \text{const}$	40
RR′C = CH — COOH	Cl_2	MeCOOH	$\lg k = -5.5\,\Sigma\sigma^+ + \text{const}$	54
$R - C_6H_4 - CH = CH -$ —COOH	Cl_2	MeCOOH	$\lg k = -3.9\,\Sigma\sigma^+ + \text{const}$	54

A linear relation has been established also between this parameter and $\Sigma\sigma^*$.[55] If two quantities are linearly related to a third, the relation between them is also linear. The application of this principle to the linear relationships involving free energy was discussed in Pal'm's monograph[56]. In the case of halogenation the principle implies that the above correlation equations represent the dependence of the rate of reaction on the ionisation potential of the alkene. The ionisation potential in turn determines the properties of the halogen–alkene molecular complexes. In this sense the correlation equations in Table 5 can be regarded as indicating a connection between reaction velocity and the properties of the complex.

3. Halogenating Agents in Polar Media

The reactivity of the halogens increases in the sequence $I_2 < Br_2 < Cl_2$. This differs from the sequence of increasing electron affinity (Table 2) and also from that of the increase in acid strength of the halogens ($I_2 > Br_2 > Cl_2$). Table 6 lists parameters representing the acidity of the halogens—free energies of formation of the corresponding trihalide ions ΔG, [57] the $X^- + X_2 \rightleftharpoons X_3^-$ equilibrium constants $K_{eq}(X_3^-)$ in sulpholan [58], and the equilibrium constants for forming the molecular complexes with benzene $K_{eq}(C_6H_6X_2)$. [59]

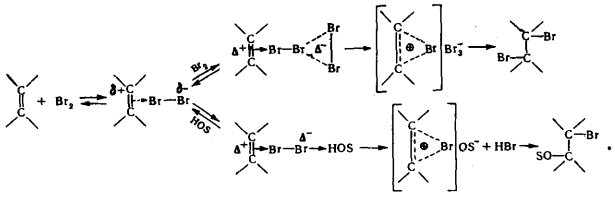
Table 6. Acidity parameters of halogens [57-59].

Hal	$-\Delta G$, kcal mole^{-1}	$K_{eq}(X_3^-)$ in sulpholan, M^{-1}	$K_{eq}(C_6H_6X_2)$, mole fractions
I_2	3.89	$10^{7.4}$	1.72
Br_2	1.67	$10^{3.8}$	1.04
Cl_2	−2.70	$10^{3.1}$	0.33

The reactivity sequence of the halogens can be explained by the participation of their cations in the reaction. The latter become more strongly electrophilic on passing from iodine to bromine and then to chlorine. The view has hitherto been held that X^+ ions act as halogenating agents in the reaction [60], but kinetic investigations have made the existence of such species improbable [61,62]. This conclusion is supported by a review on halogen cations [63]. Only cations of composition from X_2^+ to X_7^+ can exist in strongly acid media. Thus, in the absence of external additions, the only possible halogenating agents are the halogen molecules.

The reactivity of a halogen is determined by its electron affinity and molecular size. Increase in the latter weakens the Coulombic forces of attraction and prevents solvation of the transition state. The most favourable combination of these factors (Table 4) occurs with chlorine, and the least favourable with iodine. These conclusions are consistent with the observed reactivity sequence of the halogens.

The non-radical liquid-phase addition of chlorine is described by a second-order kinetic equation. Bromination in water and in methanol is also represented by a bimolecular equation, but in acetic acid third-order kinetics is observed. A termolecular equation applies in less polar media. Iodination in the absence of catalysts has a total order of three or four [1,64]. With chlorine reaction takes place readily in polar media by a simple bimolecular scheme, and does not require the action of a third particle. With bromine and especially iodine a second halogen molecule or a molecule of a hydroxylated solvent HOS is required. The gain in energy due to delocalisation of the negative charge on these particles lowers the activation energy and facilitates the reaction:



Addition of halide and other anions promotes the reactions in polar media [1]. Shilov's explanation [65] of anionic catalysis and of the action of nucleophilic solvent molecules is that the termolecular donor–acceptor mechanism involves halogenation via a transition complex in which the unsaturated molecule is subjected simultaneously to the action of electrophilic and nucleophilic reagents. The mechanism is represented by the general scheme $D \rightarrow (M \rightarrow A)$, where $(M \rightarrow A)$ is the donor–acceptor complex of unsaturated compound and acceptor (halogen) molecule, while D is an electron-donor. The transition state in the chlorination of ethylene in the presence of the chloride ion is



The simultaneous addition and removal of a chloride ion lowers the activation energy: the energy consumed in rupturing the Cl–Cl bond is balanced by the energy of formation of the C–Cl bond (Table 7).

Table 7. Activation energies for the chlorination and bromination of unsaturated compounds in acetic acid containing added lithium chloride.

Reactant	Trimethylammonium perchlorate with chlorine (Ref.42)		2,3-Dimethylpent-2-en-4-yne with bromine (Ref.66)		
LiCl, M	0	0.1	0	0.01	0.05
E_{act}, kcal mole^{-1}	7.3	4.9	7.16	6.69	5.53

The involvement of halide anions as component of the halogenating agent changes the rate law [42]. For chlorination in the presence of the chloride ion we have $W = k_3[Un][Cl_2][Cl^-]$ where Un is the unsaturated compound. Analogous equations have been established for bromination [1] and iodination [67].

Acceleration of the reaction in the presence of salts is a general feature of chlorination, and the catalytic strength of the anions is independent of their nucleophilic character [42]. The iodination of allyl alcohol in water exhibited the sequence $I^- > CNS^- > Br^- > Cl^-$. [67] Bromination is also accelerated by the addition of anions with the exception of the bromide ion, which sometimes accelerates but at other times slows down the reaction. The latter effect is explained by the binding of bromine into the tribromide anion, which is less strongly electrophilic than the free molecule. In the bromination of *trans*-stilbene in methanol the reactivity of free bromine exceeds that of the tribromide ion by a factor of 43 [68]. The ratio of their reactivities towards brominated alkenes under the same conditions varies from 5.7 to 25. [69] The activation energy for the bromination of 1,3-alkenynes is significantly higher with the tribromide ion than with molecular bromine [37]. Whereas the addition of bromide ions lowers the rate of the process with reactive alkenes, a catalytic effect is more characteristic of relatively unreactive alkenes [52,70,71]. In the bromination of several alkenes of reactivity varying by a factor of 10^7 correlations enabled anion catalysis by the bromide ion with unreactive alkenes to be separated

from inhibition of reaction due to formation of the tribromide ion with highly reactive unsaturated compounds [72]. Inhibition of chlorination by the chloride ion could not be observed because of the small equilibrium formation constant of the trichloride ion (Table 6). Thus a mechanism of polar halogenation allowing for termolecular donor–acceptor interaction provides a good explanation of the reactivities of different halogenating agents.

4. Products of Polar Halogenation

Three types of compounds—dihalides, mixed adducts (reaction involving the solvent), and monohalides (substitution)—are formed by the reaction of halogens with alkenes in polar media. Data on the composition and yields of substitution products obtained by halogenation, covering the period to 1965, were assembled in an exhaustive review by Bodrikov and Smolyan [73]. Bodrikov and his coworkers then studied the dependence of the yield and rate of formation of anomalous halogenation products on the nature of the alkene and the halogen, the temperature, the nature of the solvent, and other factors [74–77]. It was found in particular that the ratio of addition to substitution depended on the degree of charge separation in the polar transition state.

The tendency to form *trans*-dihalides falls in the sequence $I_2 > Br_2 > Cl_2$. The addition of bromine to *cis*-1-phenylpropene yields mainly the *trans*-dibromide, whereas chlorine forms a mixture of nearly equal quantities of *cis*- and *trans*-addition products [78]. The bromination of acenaphthene and phenanthrene produces the *trans*-dihalides [79,80]; chlorination gives a substantial quantity of the *cis*-adduct together with the *trans*-isomer [79,81]. Such variation is explained in terms of polar addition by the stronger tendency of bromine to form bridged structures in the cation [26]. Furthermore, the large size of iodine and bromine atoms may prevent formation of the *cis*-isomers.

Table 8. Effect of solvent on stereospecificity of bromination.

Solvnet	CCl_4	CS_2	MeCOOH	CH_2Cl_2	CCl_3COOMe	PhCN	CCl_3CN	$PhNO_2$	MeCN	H_2O
Dielectric constant ε	2.2	2.2	6.2	9.1	—	25.2	—	34.8	37.5	78.5
Percentage of *trans*-dibromide on bromination of *cis*-stilbene (Ref.88)	100	90	50	50	—	40	—	10	30	20
trans-stilbene (Ref.89)	77	31.4	—	—	51	34	34	29.5	—	—

The structure of intermediate species and of the transition state—and hence the stereochemistry of the products—depend on the nature of the unsaturated compound. Bridged structures and hence *trans*-dihalides are most probable with aliphatic alkenes. In fact the chlorination of butenes and allyl chloride in non-polar media [82] and in acetic acid [83] and the bromination of but-2-enes in acetic acid [84] are *trans*-stereospecific. Quantum-mechanical calculations show that an open carbonium ion structure is more probable for alkenes having aromatic substituents [27,85], in which stereospecificity may break down owing to stabilisation of the localised charge in the open carbonium ion. Mixtures of *cis*- and *trans*-dihalides are obtained in the chlorination of stilbenes in dichloroethane [86] and in chloroform [87], in the chlorination of 1-phenylpropenes [78], and in the bromination of substituted styrenes in acetic acid [84].

A polar mechanism provides an explanation also of the dependence of the stereochemistry of the halogenation products on the nature of the solvent. Table 8 shows that the *trans*-stereospecificity of bromination diminishes as the solvent becomes more polar. A polar solvent favours separation of charges and stabilisation of the open carbonium ion, since the energy of solvation of the latter is greater than that of the bridged structure. This leads to a decrease in the proportion of *trans*-addition.

Specific solvation may change the stereochemistry of the addition products. Thus the bromination of *cis*-β-methylstyrene in dioxan gives 80% of the *cis*-dibromide as a result of stabilisation of the unsymmetrical structure in the ion-pair by dioxan [90]. The chlorination of diphenylacetylene in benzene–pyridine mixtures yields solely *cis*-dichlorostilbene, which is explained by the cyclic structure of the transition state [91].

Table 9. Effect of solvent on relative yield of mixed chlorination products.

Solvent	ε	Ratio of yields of mixed products to dichlorides					
		pent-2-ene (Ref.92)		pent-1-ene (Ref.92)	1-phenylpropene (Ref.83)		methyl vinylacetate (Ref.93)
		cis	*trans*		*cis*	*trans*	
H_2O	78.5	—	—	—	—	—	Mixed product ∞ only
HCOOH	57.9	3.6	1.6	3.4	—	—	—
MeOH	32	10.7	5.4	11.2	4.9	4.9	—
EtOH	26.4	4.3	2.3	3.9	—	—	—
BuOH	12.3	1.0	0.45	1.4	—	—	—
CF_3COOH	8.2	0.2	0.095	0.2	—	—	0.25
MeCOOH	6.2	0.87	0.3	0.85	0.48	0.43	2.34

Halogenation results in mixed adducts when dissociated solvents (water, methanol, acetic acid) and anions of added salts are involved. Table 9 shows that the yield of mixed adducts is strongly dependent on the solvent. The quantity of mixed adducts does not correlate with the dielectric constant, and only qualitative dependence of the yield on the nucleophilic strength of the solvent is observed. It is difficult to interpret the combined effect of these two properties of the solvent. The yield of mixed products obtained by the chlorination of several unsaturated compounds [92,93] and substituted cinnamic esters [94] in acetic acid increases as the unsaturated component becomes less reactive.

According Shilov's views [5] a third component (solvent or added anion) will have an insignificant effect on the reaction if the transition state approaches an ion-pair in character. On the other hand, the less ionised the transition state the more significant the effect of the third component. In polar halogenation energy is consumed mainly in converting the π-complex into an ionised state, and in this case the involvement of a donor component, e.g. an anion, is less significant. In conformity with this,

in the presence of 1 M lithium chloride the yield of *trans*-dichloride increases in parallel with the decrease in reactivity of the double bond[94]. The predominant formation of *trans*-isomers with mixed products is connected with the synchronous action of acceptor (halogen molecule) and donor (solvent or anion) on the multiple bond. Thus kinetic examination based on the effect of non-specific solvation, the structure of the alkene, the nature of halogenating agents and third components, and also the composition of the products shows that a mechanism involving molecular complexes provides a good description of aspects of the halogenation of unsaturated compounds in polar media.

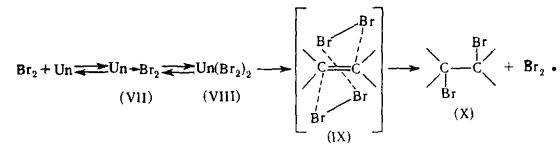
IV. MOLECULAR MECHANISM

On passing from polar to non-polar solvents the composition of the products and the kinetics of the reaction change. We must therefore examine in greater detail the mechanism of halogenation in non-polar media.

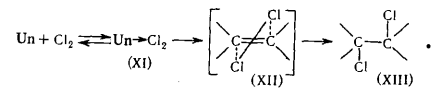
If we assume that a polar mechanism is feasible even in media of low dielectric constant, we would then expect a similar strong dependence on the structure of the alkene, since the energy barrier to a polar reaction is a linear function of the ionisation potential of the alkene. However, the rates of bromination of cyclohexene and hex-1-ene differ by a factor of 27 in methanol methanol[42], but only 4 in carbon tetrachloride[19]. The weakening of the dependence of the rate on the structure of the unsaturated compound leads to a decrease in the values of ρ in the correlation equations for non-polar media: the slope is a few negative units (Table 5) for polar media, but −0.67 for carbon tetrachloride[95]. The observed difference is inconsistent with the view that the same mechanism operates in the two cases.

A wide range of reactions in non-polar media have negative activation energies[19,96-101]: the observed values for several alkenes vary from zero to −10 kcal mole^{-1}. On the assumption that the reaction has a polar mechanism the energy barrier should be higher in such solvents as hexane and carbon tetrachloride than in polar media, but this is contradicted by experiment.

It is supposed that the bromination of ethylenic compounds can take place without the intermediate formation of ionic or strongly polar compounds[102]. Two halogen molecules and one alkene molecule are assumed to form a 2:1 complex, which can rearrange into a non-polar six-membered ring containing 4 Br + 2 C. Constructing molecular models shows that such a ring can be formed without significant distortion of the C=C and Br—Br bond lengths. Carbon and bromine atoms approach one another until relatively close to the C—Br covalent bond length, and bromine atoms from different molecules to distances close to the Br—Br bond length in the Br_2 molecule. The dibromide is formed by simultaneous rupture of two Br—Br bonds and formation of two C—Br bonds together with a new Br—Br molecule. The energy of rupture of the bonds is immediately balanced by the energy evolved on formation of the new bonds. The overall process of bromination is exothermic, so that formation of the product does not require the consumption of energy. The free-energy barrier is determined by the entropy term. If the solvent is disregarded, the hypothetical transition state contains three oriented reactant molecules, and several degrees of freedom are eliminated, so that the transition state has a large negative entropy. The product is formed from the complex by simultaneous rupture and formation of bonds. Such a reaction mechanism can be termed molecular, and represented in general by the scheme



Such a mechanism is impossible for chlorination, and the size of the chlorine molecule does not ensure formation of a structure (IX): the Cl—Cl distances in a structure similar to (IX) are so large that formation of a new chlorine molecule simultaneously with the rupture of old bonds and the formation of C—Cl bonds is not feasible. However, direct rearrangement of the complex (XI) into the reaction product is possible during chlorination:



Since the suggested chlorination transition state contains only two molecules, and its structure is less rigid than that of (IX), a lower entropy of activation and a higher rate must be expected than with bromination.

The ultraviolet spectra of mixtures of bromine with cyclohexene indicate the existence of a 2:1 complex[103], which has been demonstrated also by low-temperature infrared spectroscopy[104]. When a mixture of bromine and cyclohexene vapours is sprayed as a molecular beam on to a surface cooled in liquid nitrogen, bands due to vibrations of the double bond in 1:1 and 2:1 complexes are observed on a background of a weak band due to deformation vibration of this bond. The composition of the complexes was proved by studying the dependence of absorption on the ratio of the reactants. The displacement of the band due to the double bond is greater in the 2:1 than in the 1:1 complex, and the former has a larger heat of formation. Solid-phase conversion of the 2:1 complex into a dibromoalkane was observed when the temperature rose to −160°C. Reactants not combined in the complex are not involved in the process. A 2:1 complex has been observed also when solutions of bromine and biadamantylidene in carbon tetrachloride are mixed[105].

Table 10 lists kinetic parameters for several halogenations in non-polar media. The data for stilbenes and several other alkenes containing aromatic substituents contrast sharply with results for the remaining reactions. This is probably due to stabilisation of the positive charge by the aryl substituents, which lowers the energy of formation of the ion-pair. Since the entropy of activation of the polar reaction is numerically smaller, a polar process having an activation energy of 5–15 kcal mole^{-1} is able to compete with the molecular process. Small and negative activation energies in non-polar media correlate with the occurrence of the reactions at very low temperatures[106]. The chlorination and the bromination of cyclohexene in the absence of a solvent takes place at −175°C.[107] The chlorination of ethylene in propane takes place with considerable velocities between −140° and −150°C.[108]

A negative temperature coefficient is a general feature of the addition of halogens to alkenes in non-polar media. It is not connected with the temperature dependence of the pre-exponential factor. The activation energy observed for an elementary termolecular reaction is given by the difference between the true height of the barrier and $4RT$, and the appearance of this difference is associated with

the pre-exponential factor. At 300°K we have $4RT \simeq 2.4$ kcal mole^{-1}, which does not explain the experimental values of the negative temperature coefficient.

Table 10. Kinetic parameters of some halogenations in carbon tetrachloride at 25°C.

Alkene	Hal	Overall order	Rate constant	Activation energy, kcal mole^{-1}	Ref.
Cyclohexene	Br_2	3	8 M^{-2} s^{-1}	-8.0	19
Hex-1-ene	Br_2	3	1.5 M^{-2} s^{-1}	-4.1	19
4-Methylpent-1-ene	Br_2	3	1.5 M^{-2} s^{-1}	-3.5	19
Diphenylalkenes	Br_2	3	20-150 M^{-2} s^{-1}	0--5	100
Hex-1-ene	Cl_2	2	0.013 M^{-1} s^{-1}	0	99
Cyclohexene	Cl_2	2	0.15 M^{-1} s^{-1}	-1.7	99
Cyclohexene	IBr	3	45 M^{-2} s^{-1}	-8.2	98
cis-Stilbene	Br_2	3	-	+6.5	12
trans-Stilbene	Br_2	3	0.032 M^{-2} s^{-1}	+13.9	12

The observation of negative activation energies may be evidence that molecular complexes are involved in the reaction mechanism. If the kinetic equations for a scheme of the type $Un + X_2 \rightleftharpoons \pi$, $Un + X_2 \rightarrow P$ (where π is the complex and P the product) with parallel formation of the complex are differentiated with respect to the reciprocal of the temperature, the resulting equation is

$$E_{obs} = -R\frac{\partial \ln k_{obs}}{\partial T^{-1}} = -R\frac{\partial \ln k_2}{\partial T^{-1}} + R\frac{\partial}{\partial T^{-1}}(1 + K_{eq}[Un] = \\ = E_2 + \frac{K_{eq}[Un]}{1+K_{eq}[Un]}|\Delta H| > 0 \quad (3)$$

where E_{obs} is the experimental activation energy, E_2 the true activation energy of the bimolecular reaction between halogen and alkene, $|\Delta H|$ the numerical value of the enthalpy, and K_{eq} the equilibrium constant of complex formation. Equation (3) shows that, at sufficiently high alkene concentrations [Un], the observed activation energy increases from E_2 to $E_2 + |\Delta H|$ with increase in this concentration. A similar increase is observed on passing from high temperatures ($K_{eq} \rightarrow 0$) to low temperatures ($K_{eq} \gg 1$). Thus increase in K_{eq}[Un] should be accompanied by a gradual increase in the activation energy, and

$$E_{obs}^{max} - E_{obs}^{min} = |\Delta H| \ . \quad (4)$$

For a termolecular scheme not involving the complex we have

$$E_{obs} = E_3 + \frac{2K_{eq}[Un]}{1+K_{eq}[Un]}|\Delta H| > 0 \\ \text{and } E_{obs}^{max} - E_{obs}^{min} = 2|\Delta H| \ . \quad (5)$$

For the simplest bimolecular scheme involving a π-complex we find that

$$E_{obs} = E_2 - |\Delta H| + \frac{K_{eq}[Un]}{1+K_{eq}[Un]}|\Delta H| \ . \quad (6)$$

If $E_2 > |\Delta H|$, this case is identical with the parallel scheme. But when $E_2 < |\Delta H|$, a negative temperature coefficient must be expected in the region of small values of the product K_{eq}[Un] (low concentrations and not too low temperatures). The numerical value of this coefficient will decrease at low temperatures and with increase in [Un], and at some point the coefficient will become positive. Here, as before, Eqn. (4) holds. Fig. 3 illustrates various forms of temperature dependence of the rate constant for the given scheme.

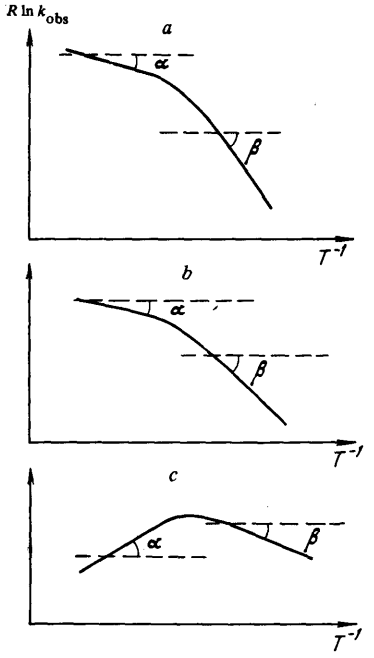


Figure 3. Possible forms of temperature dependence of the effective rate constant of bimolecular halogenation.

For the corresponding termolecular scheme we have

$$E_{obs} = E_3 - |\Delta H| + \frac{2K_{eq}[Un]}{1+K_{eq}[Un]}|\Delta H| \ . \quad (7)$$

With $E_3 < |\Delta H|$, low concentrations [Un], and sufficiently high temperatures a negative temperature coefficient may be expected even for termolecular reactions. Maximum and minimum values of the activation energy are connected by the relations (5).

The negative temperature coefficient may increase when two types of complexes (e.g. 1:1 and 2:1) are involved in the reaction. For a termolecular scheme and a steady state with respect to both complexes we have $E_{obs} = E_3 - (|\Delta H| + |\Delta H'|)$, where $|\Delta H'|$ is the enthalpy of formation of the 2:1 complex. The difference between maximum and minimum values of the observed activation energy is $2(|\Delta H| + |\Delta H'|)$. If a steady state with respect to the second complex is established slowly, the situation is more complicated. The product will accumulate in conformity with an autocatalytic law, and a negative temperature coefficient may not be observed under these conditions even when $E_3 < (|\Delta H| + |\Delta H'|)$.

Thus schemes that involve parallel formation of a molecular complex are unable to explain the appearance of a negative temperature coefficient. Such a possibility is feasible with a complex as a reaction intermediate. A negative activation energy therefore provides kinetic evidence that complexes are involved. Negative activation

energies indicate that the potential energy of the transition state during halogenation lies below that of the initial molecules. According to the theory of the activated complex maximum free and potential energy corresponds to the transition state. Fig. 4 shows possible changes in potential and free energy along the reaction path for the halogenation of alkenes in non-polar media. In the case illustrated the potential energy has a maximum in the transition state, but is lower than in the initial molecules. This means that the formal activation energy in the Arrhenius equation becomes less than zero for the effective rate constant. Observed activation energies close to zero can be expected for chlorination. Large negative values are possible for the entropy of activation, especially in the case of bromination, and reaction velocities will be low. All the above features are in fact confirmed by experimental data [19,102].

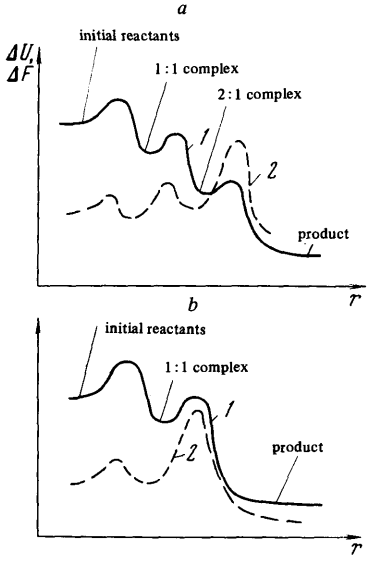


Figure 4. Variation of: 1) potential energy; 2) free energy along path of molecular reaction: *a*) bromination; *b*) chlorination.

Specific solvation of starting materials and transition state should play an important part in a molecular mechanism. The formation of complexes with halogens is typical of several compounds used as solvents (Table 11). Crystalline molecular compounds of carbon tetrachloride with chlorine are known [119]. A charge-transfer band between carbon tetrachloride and bromine in perfluoropentane solution has been detected spectrophotometrically [120].

The dissolution of any substance A in a solvent S is accompanied by solvation and the formation of a solvate complex of mean composition AS_n:

$$(A)_{S,L,G} + nS \rightleftarrows AS_n .$$

Strictly speaking, all the substance A is present in solution as such a solvate complex AS_n. The formation in solution of a complex of a halogen with a donor, e.g. an alkene, can be represented:

$$X_2S_n + D \overset{K_{eq}}{\rightleftarrows} X_2{\cdot}D + nS \qquad K_{eq} = \frac{[X_2D][S]^n}{[X_2S_n][D]} . \qquad (8)$$

Table 11. Enthalpies of formation ($-\Delta H$, kcal mole^{-1}) of molecular complexes of halogens with certain donor solvents.

Hal	Benzene	Toluene	Methanol	Dioxan	Dimethyl sulphoxide	Oxolan	Pyridine	Diethyl ether
I_2	1.3[109]	1.8[109]	1.9[110]	3.3[111]	3.7[114]	5.3[115]	7.8[116]	4.3[117]
Br_2	—	—	—	2.0[112]	—	3.5[112]	—	5.5[118]
Cl_2	—	—	—	2.1[113]	—	2.5[113]	4.3[113]	—

The applicability of Eqn. (8) has been shown [121] for the ternary systems formed by iodine and hexane with benzene, tetrachloroethylene, carbon tetrachloride, and allyl bromide and by iodine with benzene and carbon tetrachloride. In all cases 1 : 1 complexes are formed, which confirms the type of interaction between halogens and solvents.

Reaction may be prevented by formation of a halogen–solvent donor–acceptor bond. The acceptor and electrophilic properties of a halogen become weaker when it is bound into a complex. Formation of the complex X_2.Un by the exchange reaction (8) is impeded by the presence of a bond with the solvent. Increase in the donor strength of the solvent is accompanied by a rise in the potential barrier to complex formation: for example, the enthalpy of interaction of bromine with dimethyl sulphide is -9 kcal mole^{-1}, [112] and up to 10 kcal mole^{-1} is absorbed by reaction (8) in this case. In such solvents the formation of complexes may become the limiting stage, and the reaction velocity may be lower than in weakly complexing solvents such as carbon tetrachloride. In fact, hardly any bromination of alkenes occurs in dimethyl sulphide [118]. Donor solvents are able to solvate not only the halogens but also the transition state. The role of such solvation in effecting the reaction has been noted several times by Shilov [5,65]. Solvation of the transition state, like that of the initial molecules, depends on the donor strength of the solvents. Cases are probable in which solvation of the transition state will exceed that of the reactants. The reaction velocity may increase in such solvents. The relative strength of solvation effects in the reaction can be assessed from the enthalpy of the various processes involved in complex formation, and the reaction velocity may be expected to pass through a maximum depending on the stability of the halogen–solvent complex. This phenomenon has been observed in the bromination of cyclohexene and hex-1-ene in solvents that form complexes with bromine [118] (Fig. 5). The maximum rate of reaction is found in dioxan. A similar relation has been obtained for iodination–cyclisation [122], where the iodine–benzene complex exhibited the maximum rate.

A molecular mechanism should yield *trans*-addition products, which has been confirmed experimentally [99,102,123]. Breakdown of stereospecificity on passing to more polar media has been reported [78,88], and is probably due to a diminution in the contribution by the molecular mechanism.

In several cases specific solvation effects are as important as the dielectric constant of the medium. The concentration of added bromobenzene appears in the rate equation for the bromination of stilbenes in carbon tetrachloride, and the activation energy falls from 13.9 to 8 kcal mole^{-1} on the addition of 10% of bromobenzene [124].

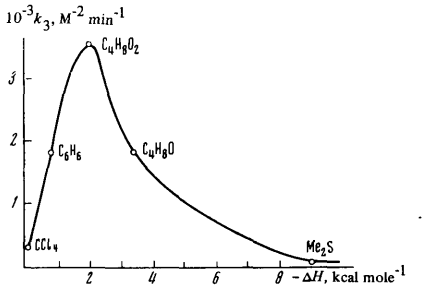


Figure 5. Dependence of rate constant for the bromination of hex-1-ene on enthalpy of formation of bromine–solvent molecular complex.

In mixtures of carbon tetrachloride and nitrobenzene the chlorination rate constant increases considerably more rapidly than might be expected from the variation in the dielectric constant of the medium [125]; this is explained by specific solvation of chlorine by nitrobenzene. This polarises the chlorine molecule, which facilitates electrophilic attack on the double bond. Catalysis of chlorination in carbon tetrachloride and benzene by carboxylic acids is also related to specific solvation [91], and becomes greater as the acid becomes stronger. Only the monomeric forms of the acids are active. A probable mechanism for the action of carboxylic acids is solvation of the anionoid part of the transition state by the proton.

Thus the halogenation of alkenes in non-polar media is characterised by negative effective activation energies and high kinetic orders. The reaction velocity depends on the specific solvation of the halogens. All these facts are consistent with the view that various donor–acceptor complexes are involved in the reaction, and are converted into the reaction products by a molecular mechanism.

V. RADICAL MECHANISM

The gas-phase halogenation of alkenes takes place by a radical–chain mechanism [126]. For a long time no attention was paid to radical halogenation in the liquid phase. The Review discusses radical halogenations taking place at normal temperatures in the absence of illumination and catalysts. Such a reaction (bromination) was first studied in 1951. [127] The process is sharply retarded by inhibitors and by contact with an extended glass surface. Toluene, which is stable towards the short-term action of bromine, reacts with the latter in the presence of an unsaturated compound. The *trans*-addition product is formed under conditions favouring a polar reaction. Nearly equimolecular proportions of *trans*- and *cis*-dibromides are obtained in carbon tetrachloride. Criteria enabling radical halogenations to be identified were formulated [127]—action of inhibitors, nature of products obtained under various reaction conditions, entry into reaction of reactants that are stable towards the halogen in the absence of an unsaturated compound.

The radical chlorination of alkenynes induces benzene and tetrachloroethylene to enter into reaction [128]. Poutsma demonstrated that the chlorination of cyclohexene proceeds partly by a radical mechanism [129]. The postulate of a radical mechanism explained the chlorination of aromatic and saturated hydrocarbons induced by alkenes [130–132]. Radical chlorination is not a consequence of chance external initiation but depends on the chemical nature of the reactants [133]. A radical mechanism is characteristic of the bromination of dienes [134,135], cyclohexene [103], hex-1-ene, and *p*-allylbromobenzene [101].

The proportion of radical processes is determined by the structure of the alkene. An unbranched chain confers the greatest tendency to radical chlorination, but branched alkenes—isobutene, tri- and tetra-methylethylenes, and also styrene—are not characterised by a radical reaction [123]. The reaction mechanism is affected also by the concentration of the alkene: the chlorination of cyclohexene becomes almost exclusively a radical reaction as the concentration of the hydrocarbon increases, and the proportion of the non-radical process increases with decrease in the concentration [133]. A similar phenomenon has been observed in the bromination of hex-1-ene [101], butadiene [135], and *cis*- and *trans*-penta-1,3-dienes [136]. Styrene, which is chlorinated and brominated in conformity with a non-radical scheme, reacts with iodine by a purely radical mechanism [137]. Oxygen inhibits radical chlorination [123], bromination [101,103], and iodination [137]. The scheme

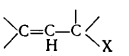
$$StI^{\cdot} + O_2 \rightarrow StIO_2^{\cdot},$$

$$2StIO_2^{\cdot} \rightarrow IStOOStI + O_2,$$

$$StIO_2^{\cdot} + StI^{\cdot} \rightarrow IStOOStI,$$

was suggested [137] for inhibition of the iodination of styrene (St). The action of oxygen is twofold: small additions of oxygen initiate the bromination of tetrachloroethylene, but excess slows it down [138]. Radical halogenation is inhibited also by quinones [137], substituted phenols [136], and cyclohexene oxide [139].

The radical bromination of cyclohexene gives the dibromide in yields exceeding 90%, [103] and hex-1-ene gives a 50% yield [19]. The dihalide is usually the *trans*-product contaminated with the *cis*-isomer. The chlorination of cyclohexene gives more than 95% of the *trans*-dichloride. The bromination of cyclohexene [102] and photochemical iodination of butenes [140] and pentenes [141] are *trans*-stereospecific. In several cases, however, stereospecificity is absent [127,136]. Radical halogenation also yields substitution products, whose proportion sometimes reaches 50%. Substitution products containing an allyl group



are most usual. Allylic compounds are formed in yields of 50%, 27%, and more than 40% in the isobutene–chlorine, cyclohexene–chlorine, and hexene–bromine systems respectively. Vinyl halides, containing halogen at the double bond, are always formed in small amounts (from fractions to 5%). Considerable quantities of the 4-halogeno-derivative are observed in the reaction of chlorine with but-1-ene [123] and in the bromination and chlorination of cyclohexene [103,133]. Products of the latter type are found only in radical halogenation.

Published kinetic data on radical halogenation are collected in Table 12, which shows such reactions to have low and negative effective activation energies, from −15 to 6.5 kcal mole^{-1}. The kinetic equations are extremely diverse. The quantity of data on radical liquid-phase halogenation is limited, and further investigation of these reactions is required.

Table 12. Radical-chain halogenation of alkenes in carbon tetrachloride.

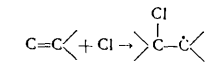
Alkene	Hal	Kinetic equation	Activation energy	Ref
4-Methylpent-1-ene	Br_2	$k[Un][Br_2]^2$	−15	19
Hex-1-ene	Br_2	$k[Un]^2[Br_2]^{3/2}$	−8	19
Cyclohexene	Br_2	$\begin{cases} k[Un][Br_2]^2 \\ k[Un]^2[Br_2] \end{cases}$	−14	19
p-Allylbromobenzene	Br_2	$k[Un]^2[Br_2]$	0	101
Pentenes	I_2	$\frac{k_1[I_2]^{3/2}[Un]}{1+k_2[Un]}$	no data	141
Styrene	I_2	$k[Un]^{3/2}[I_2]$	+6.5	137

Halogenation in the dark is initiated by the alkene, not by thermal breakdown of the halogen molecule into two atoms. Aromatic and saturated hydrocarbons that are inert towards the halogen react in the presence of alkenes [130-132]. If the alkene were not involved in initiation, the rate of initiation would be independent of its presence, and the degree of halogenation of the aromatic or saturated compound would also have been constant. Actually, however, it differs by several orders of magnitude [128], which proves that more halogen atoms are formed in the presence than in the absence of alkenes. Comparison of possible rates of initiation with the observed reaction velocities also shows that the latter cannot be attained with actual chain lengths and with initiation by the dissociation of halogen molecules.

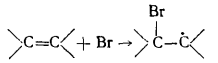
Table 13. Heats of initiation in halogen-alkene systems.

Initiation reaction		Heat of reaction, kcal mole^{-1}	
		bromine	chlorine
$-CH=CH- + X_2 \rightarrow -CHXC\dot{H} + X$	(9)	34	32
$2-CH=CH- + X_2 \rightarrow 2-CHX-C\dot{H}-$	(10)	22	6
$-CH=CH- + 2X_2 \rightarrow -CHX-CHX- + 2X$	(11)	14	8
$2-CH=CH- + 2X_2 \rightarrow -CHX-CHX- + X + +-CHX-C\dot{H}$	(12)	3	−18
$-CH=CH-CH_2- + X_2 \rightarrow HX + X + -CH= =CH-C\dot{H}-$	(13)	32 (35)	29 (32)
$2-CH=CH-CH_2- + X_2 \rightarrow 2HX + 2-CH= =CH-C\dot{H}-$	(14)	18 (24)	0 (+6)

With regard to possible schemes of initiation involving the alkene Table 13 gives several mechanisms of radical generation in the presence of bromine and chlorine, together with probable heats of reaction for these processes. The latter were estimated from the energies of rupture of bonds in the halogen molecules (Table 2). The thermal effect of the reaction



was equated to the heat evolved on attachment of a chlorine atom to ethylene, i.e. 26 kcal mole^{-1}. [133] In most compounds the C-Br bond is less stable than the C-Cl bond by 14 kcal mole^{-1}, and for the reaction



it was assumed that ΔH = 12 kcal mole^{-1}. The energies of formation of hydrogen chloride and hydrogen bromide are respectively 103 and 88 kcal mole^{-1}. [21] The heat of detachment of hydrogen in the allyl position was taken [133] to be 74 kcal mole^{-1}, but the values in parentheses in Table 13 are based on the more usual 77 kcal mole^{-1}. The C-Cl and C-Br bond energies are respectively 80 and 66 kcal mole^{-1}. [21]

The results for the heats of reaction enable reactions (10) and (14) to be eliminated for bromine, since both these routes are less favourable than (11). Bimolecular initiation according to (9) and (13) is energetically identical in the case of bromine. Thus three schemes of initiation—bimolecular with ΔH_{13} = 32-35 kcal mole^{-1}, termolecular with ΔH_{11} = 14 kcal mole^{-1}, and formally quadrimolecular with $\Delta H_{12} \simeq 3$ kcal mole^{-1}—can be considered for bromination. A similar analysis for chlorine gives corresponding values of 29-32, < 8, and −12 kcal mole^{-1}. [142] The pre-exponential factors of bimolecular and termolecular reactions can be taken to be 10^{10} M^{-1} s^{-1} and 10^4 M^{-2} s^{-1}. [142] With reactant concentrations each of 0.03 M at 25°C we find that the bimolecular reaction may generate radicals at rates of 10^{-17} and 10^{-14} M s^{-1} for bromine and chlorine respectively, the corresponding rates for the termolecular reaction being 10^{-13} and 10^{-5}. Stage (12) can be regarded as the collision of two molecules of the complex $\cdot X_2.Un$, when rates of initiation may be higher than in the remaining cases. In order that reaction (12) should occur four reactant molecules must be oriented in a certain way, which may lead to great steric hindrance.

The formation of radicals as a result of the interaction of valency-saturated molecules by bimolecular and termolecular mechanisms has been thoroughly studied in the liquid-phase oxidation of hydrocarbons [143]. A termolecular mechanism predominates with hydrocarbons having weak C-H bonds. It is very likely that termolecular and pseudo-quadrimolecular are more efficient than bimolecular reactions also in the halogenation of alkenes. A review has been devoted to the possible role of molecular complexes in the formation of radicals [144]. Complex formation may weaken the bond in the acceptor molecule. Such a mechanism has been proved for the formation of radicals from tetranitromethane complexes [145]. It has been accepted [133] that the first stage in chlorination is always formation of a complex $Cl_2.Un$, which then breaks down either by a homolytic or by a heterolytic mechanism. The involvement of complexes in the reaction has been assumed also for radical bromination [101,135] and iodination [137]. Hitherto, however, there has been no unambiguous experimental evidence in halogenation reactions that complex formation should precede the formation of radicals.

The participation of complexes in halogenation explains the parallel variation in the reactivity of alkenes in polar, molecular, and radical reactions. If a complex is an

intermediate species in all these processes, the rate constants should actually correlate with the properties of the complex and thus also among themselves. Pseudo-quadrimolecular initiation must be regarded as resulting from pair collisions of 1 : 1 complex molecules.

In radical halogenation chain propagation can be effected by the reactions

$$X + -CH=CH-CH_2- \rightleftarrows -CHX-C\dot{H}-CH_2- , \quad (15)$$

$$X + -CH=CH-CH_2- \rightleftarrows HX + -CH=CH-C\dot{H}- , \quad (15')$$

$$-CHX-C\dot{H}-CH_2- + X_2 \rightarrow -CHX-CHX-CH_2- + X , \quad (16)$$

$$-CH=CH-C\dot{H}- + X_2 \rightarrow -CH=CH-CHX- + X . \quad (16')$$

The activation energies of (15) and (15′) can be estimated by means of the formulae—$E_{act} = 4.3 - 0.1\Delta H$ in an exothermic reaction, and $E_{act} = 4.3 + 0.91\Delta H$ in an endothermic reaction [146]—and in the case of chlorine we have $E_{act} = 2$ kcal mole^{-1} for reaction (15). The pre-exponential factors of the gas-phase reactions of the atoms with the ethylenic compounds amount to 10^{12} M^{-1} s^{-1}, [147]† which gives $k_7 = 10^{10}$ M^{-1} s^{-1}, in good agreement with the experimental $10^{9.9}$ M^{-1} s^{-1}. [148] The heats of reaction of stages (15) and (15′) differ by 2–3 kcal mole^{-1}, and the corresponding rates differ little. As a consequence, the dihalide is accompanied by large quantities of substitution products. In the case of bromine we have $k_7 \simeq 10^8$–10^9 M^{-1} s^{-1} for reactions (15) and (15′). The estimated rates of reactions (16) are of the same order. The rate of (16) may be lower than the calculated value because of steric hindrance to reaction of the halogenalkyl radical with the molecule. The most feasible value in this case is 10^7–10^8 M^{-1} s^{-1}. The rate of reaction (16′) is lower, since its heat of reaction is 5 kcal mole^{-1}. The reversibility of stage (15) is a very important matter, and may affect the kinetics of the process. With chlorine this stage is irreversible, since the reverse reaction is strongly endothermic. With bromine, on the other hand, the decomposition constant of the halogenoalkyl radical is estimated to exceed 10^6 s^{-1}. At a halogen concentration of 0.01 M this decomposition is able to compete with reaction (16).

Halogen atoms, which possess high electron affinities, are very strong acceptors and form complexes with organic donors such as benzene [149]. The enthalpy of formation of such complexes is about double those of complexes of the corresponding molecular halogens [150]. Such complexes should be formed also with alkenes, and the enthalpy can be expected to be 6–12 kcal mole^{-1}. The intermediate species in halogenation may not be classical halogenoalkyl radicals but radical-like complexes



distinguished by the position of the atom and by delocalisation of the free valency over a three-membered ring [103,140]. In fact the heat evolved on formation of a classical radical is smaller with iodine, but with bromine is close to that evolved on formation of the complex. The latter does not require rupture of the double bond, so that formation of such a complex may not have an activation barrier, in contrast to the reaction yielding



A bridged structure for the halogenoalkyl radicals is supported by the *trans*-stereospecificity of the radical addition of bromine and iodine [140]. If the reaction involved the radical



it would not have been completely *trans*-stereospecific with iodine, and with bromine there would have been no advantage at all in formation of a *trans*-product, as is observed e.g. in ionic reactions of the geometrically entirely similar cation [1]



Thus the most probable structure with bromine is



The reversibility of stage (15) can be regarded as a consequence of complex formation between the bromine atom and the unsaturated compound. With chlorine, formation of the complex involves a smaller—and that of the radical a larger—heat of reaction than with bromine, so that the radicals



play the main part in the reaction.

Complex formation explains negative activation energies in radical bromination, since the enthalpy of formation of the radical–complex occurs in the activation energy with a negative sign [116]. A negative activation energy due to reversible formation of a bromoalkyl radical has been reported for the gas-phase hydrobromination of alkenes [151].

Chain termination takes place either by the recombination of atoms and radicals or by reaction with an inhibitor (In):

$$2X \rightarrow X_2 , \quad (17)$$

$$X^{\cdot} + \dot{C}-C(X) \rightarrow \text{Products} , \quad (17')$$

$$2\,\dot{C}-C(X) \rightarrow \text{Products} , \quad (17'')$$

$$\left.\begin{array}{l} X + In \rightarrow \text{Termination} \\ \dot{C}-C(X) + In \rightarrow \text{Termination} \end{array}\right\} . \quad (18)$$

Only the rate constants of reaction (17)—$10^{10.6}$ and $10^{10.3}$ M^{-1} s^{-1} for bromine and iodine [148] respectively—are known for the liquid phase. The rates of reactions (17′) and (17″) are apparently lower owing to steric hindrance. This is supported by data for the gas phase, where $k_{17} = 10^{16}$–10^{17} M^{-1} s^{-1} for chlorine‡, the reaction Cl + C_2H_4Cl gives only 10^{14}, and the recombination of two chloroethyl radicals only 10^{13}. [147] Mechanism (18) is more probable. Furthermore, chain termination may take place on oxygen, which is usually present in solution at concentrations of $\sim 10^{-3}$–10^{-4} M. Radical halogenation is complicated by liberation of the hydrogen halide, which influences the kinetics of the reaction.

†The pre-exponential factors given in Ref. 147 are $\sim 10^{12}$ cm^3 mole^{-1} s^{-1} (Ed. of Translation).

‡This value of k_{17} is in fact the third-order rate constant in cm^6 mole^{-2} s^{-1}, and the two subsequent rate constants are in cm^3 mole^{-1} s^{-1}, although the units are not stated in the Russian text (Ed. of Translation).

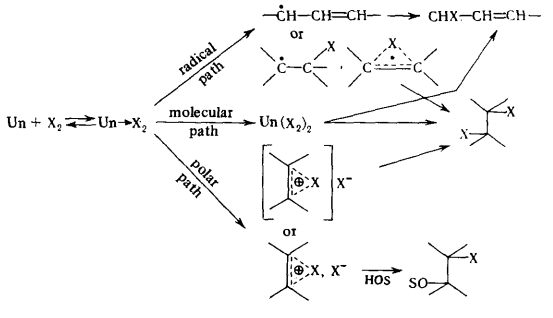
The detailed mechanism of radical halogenation cannot yet be regarded as finally established. Complexes of halogen atoms with alkenes can be assumed to take part in the reaction: without this hypothesis the stereochemistry of the products of radical halogenation becomes incomprehensible.

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Published information on the addition of halogens at a multiple bond shows the attention hitherto devoted to this reaction by research workers. Addition processes occur mainly in organic chemistry. They have formed the basis, in particular, for developing the concepts of carbonium ions, electrophilic and nucleophilic reagents, and π-complexes. The hydrohalogenation of alkenes has played an important part in establishing and developing the chemistry of free radicals.

The Review has considered the halogenation of multiple bonds mainly from the point of view of the possible role of halogen–alkene molecular complexes in this process. The existence of such complexes has been demonstrated experimentally, but their part in halogenation has been inadequately studied. Involvement of molecular complexes in the chemical change enables a unified view to be taken of the mechanism of halogenation. Available information can be summarised by Scheme 3.

Scheme 3.



The concept of complexes will explain the acceleration of the reactions with fall in temperature, the rapidity of the process in non-polar media and at low temperatures, the effect of specific solvation, and several other features of the reaction in systems where donor–acceptor interaction exists between the initial substances, but takes no direct part in the reaction.

The halogenation of multiple bonds shows that, depending on the properties of the medium and the reactants, subsequent changes in the complex can take place by ionic, radical, or molecular mechanisms. The investigation of such processes provides an approach to solving one of the problems of present-day chemical kinetics—elucidating the kinetic role of various types of complexes in chemical reactions. Examination of problems connected with this concept shows the absence of sharp distinctions between ionic and radical reaction mechanisms. Direct conversion of the complexes into the final products is also a possibility. The occurrence of such processes is of fundamental interest.

The halogenations of unsaturated compounds and in particular of alkenes have low activation energies. The reaction can take place in an inert phase over the temperature range 77–400°K, which enables individual stages in the process to be isolated and studied. The fact that the activation energy is comparable with the enthalpy of complex formation makes the halogenation of alkenes a convenient model for studying several general aspects of the effect of complex formation on a chemical process. New opportunities for controlling the rate and enhancing the selectivity of the most diverse processes are opened up by studying complex formation between reactants and paths for the further transformation of the complexes.

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Lomonosov Moscow State University

Institute of Organic Chemistry,
Ukrainian SSR Academy of Sciences,
Kiev

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The Radical-anions and Dianions of Aromatic Hydrocarbons in Metallation Reactions

E.S.Petrov, M.I.Terekhova, and A.I.Shatenshtein

The review gives a general account of the literature data on the behaviour of the radical-anions and dianions of aromatic hydrocarbons in reactions involving the metallation of aliphatic-aromatic compounds and discusses the mechanisms of these reactions, the role of the counterion, the degree of its solvation, and the type of ionic association complexes in solutions of the reactants being emphasised. Since the carbanions of dihydro-derivatives of aromatic hydrocarbons are formed in the course of the reactions, data are presented also on their involvement in the metallation processes. The relative propotophilic properties of the three types of metallating agents, established experimentally and determined from the localisation energies of their protonation reactions calculated by the Pariser-Parr-Pople method, are compared.
The bibliography includes 120 references.

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I. REACTIONS OF RADICAL-ANIONS AND DIANIONS AS REDUCING AGENTS AND BASES

Radical-anions (r.a.) of aromatic hydrocarbons are usually obtained in solution by electrochemical reduction at the cathode or by chemical reaction with an alkali metal [1,2]. Under favourable conditions, there is a possibility of the transfer of two electrons to the hydrocarbon molecule and the formation of a dianion (d.a.); trianions are generated much more rarely. The role of radical-anions and dianions in organic chemistry is very great and much attention has been devoted to the study of their formation, structure, properties, and reactivities (see the relevant reviews[1-13]).

As a result of intense study in recent years, it has been established that the transfer of one electron with formation of a radical-anion is the first step in many reactions (see the relevant reviews [9,11,14]). Such are, in particular, the reactions involving the metallation of aliphatic-aromatic compounds by alkali metals. The capacity of radical-anions to give up readily the unpaired electron in the non-bonding orbital of the aromatic hydrocarbon to compounds with a higher electron affinity permits numerous reduction reactions, including the sensitisation of anionic polymerisation leading to the formation of "live" polymers [7]. The protophilic properties of radical-anions are a consequence of the enhanced electron density at their carbon atoms. Dianions are more vigorous reducing agents and proton acceptors than radical-anions [15]. Adducts of aromatic hydrocarbons with alkali metals, which include radical-anions or dianions in their composition, have been used successfully for the metallation of a wide variety of organic compounds [16-20], behaving as proton acceptors, i.e. bases.

A mechanism of the protonation of aromatic radical-anions and dianions has been proposed by Laitinen and Wawzonek [21] and Hoijtink et al. [15], in relation to the electrochemical reduction of aromatic hydrocarbons (Ar) in aqueous dioxan. Initially the interaction of the primary reduction product, the radical-anion Ar^-, with the donor BH entails the formation of the radical ArH$^\cdot$:

$$Ar^- + BH \rightarrow ArH^\cdot + B^- . \quad (1)$$

Since it has a higher electron affinity [15], ArH$^\cdot$ combines with an electron and is converted into the carbanion of the dihydro-derivative of the aromatic hydrocarbon ArH^-:

$$ArH^\cdot + Ar^- \rightarrow ArH^- + Ar . \quad (2)$$

Apart from the radical-anion, the metal, cathode, etc. can behave as the electron donor. In the final stage, a proton adds to the carbanion and the dihydro-derivative is obtained:

$$ArH^- + BH \rightleftarrows ArH_2 + B^- . \quad (3)$$

Usually the rate of electron transfer [reaction (2)] is higher by several powers of ten than the rate of protonation [22] [reactions (1) and (3)].

The protonation of the dianion includes the stage involving the formation of ArH^-:

$$Ar^{=} + BH \rightleftarrows ArH^- + B^- \quad (4)$$

and then ArH_2:

$$ArH^- + BH \rightleftarrows ArH_2 + B^- . \quad (5)$$

The protonation of radical-anions and dianions of different structures by water, alcohols, and acids has been considered by a number of workers [23-35]. Weissman and coworkers [23] adopted the mechanism (1)–(3) for the reaction of sodionaphthalene with water. Its validity was demonstrated by Bank and Closson [25] using an isotopic method. Regardless of the rate of addition of tritiated water to the solution of sodionaphthalene in tetrahydrofuran (THF), a mixture of naphthalene, dihydronaphthalene, and a small amount of tetralin was obtained and only the last two products were radioactive.

In the discussion of this result, Bank and Closson noted that, if reaction (1) were followed by the disproportionation of the radicals ArH$^\cdot$,

$$ArH^\cdot + ArH^\cdot \rightarrow ArH_2 + Ar , \quad (6)$$

naphthalene would have been radioactive too.

Presumably the radical-anion could disproportionate initially:

$$Ar^{\cdot-} + Ar^{\cdot-} \rightleftarrows Ar^{=} + Ar, \quad (7)$$

and then the dianion would be protonated via reactions (4) and (5). Then, when the required amount of water is added slowly, one should expect the involvement of $Ar^{=}$, ArH^{-}, and Ar in the equilibrium. However, naphthalene would contain tritium under these conditions. Since there is no tritium in naphthalene, the mechanism (1)–(3) is correct.

The formation of the carbanions ArH^{-} in the reaction with the proton-donating dianions of a number of aromatic hydrocarbons was demonstrated spectroscopically by Velthorst and Hoijtink [26]. Krapcho and Bothner-By [36] applied the mechanism of the protonation of a radical-anion to the hydrogenation of organic compounds by an alkali metal in liquid ammonia with added alcohol (the Birch reaction). In liquid ammonia, the alkali metal M is ionised [37]:

$$M \xrightarrow{NH_3} M^{+} + e^{-}, \quad (8)$$

the cation and the electron (e^{-}) being solvated by ammonia. The addition of one or two electrons to the molecule of the organic substance converts it into a radical-ion or dianion, which then reacts with the alcohol [reactions (1)–(5)]. In addition to the dihydro-derivative, more highly hydrated compounds are frequently formed (see the relevant reviews [37-41]).

Eisch and Kaska [18] suggested that the metallation of aliphatic-aromatic hydrocarbons (in particular tri- and di-phenylmethane) by an adduct of an aromatic hydrocarbon and an alkali metal (lithiobiphenyl) takes place similarly, i.e. via stages (1)–(3). This mechanism of metallation, involving radical-anions, is now generally accepted.

When the acidity of the proton donor BH is low (for example, when BH is a CH acid), the protonation may not go to completion owing to the reversibility of reactions (3)–(5). When Ar is a polycyclic hydrocarbon, an equilibrium is frequently established in the disproportionation reaction of two carbanions of the dihydro-derivative [25,42]:

$$ArH^{-} + ArH^{-} \rightleftarrows ArH_2 + Ar^{=}. \quad (9)$$

The protonation (metallation) process can also be complicated by electron transfer from the radical-anion or the dianion to the proton donor [19,43,44]:

$$Ar^{\cdot-} + BH \rightleftarrows Ar + BH^{\cdot-}. \quad (10)$$

The mode of reaction depends on factors such as the ionisation potential and the protophilic properties of the radical-anion or dianion, and the acidity and electron affinity of the proton donor. Cations, which are not indicated in the above reactions, and solvents in which the reactions are carried out play an important role. The position of equilibrium in the formation of the radical-anions and their conversion into dianions by reduction or disproportionation depend to a considerable degree on the counterion and the solvent [5,7]. Nevertheless, in certain cases the last reaction may actually cause the protonation of the dianion and not the radical-anion, as shown by Szwarc and coworkers [35] for the perylene radical-anion.

Like other anionic organic reactions, the metallation processes involving radical-anions and dianions are frequently carried out in ethereal solvents, since the latter are very weak proton donors and effectively solvate the cations. Since the dielectric constants (DC) of ethers are low, (3–7 at 25 °C), ionic association effects are often of primary importance. In a general form, the equilibrium between the individual states of the organic derivative of the alkali metal (AM) in solution is described by mechanism (11), [45,46] which does not, however, take into account the solvation of the species:

$$(A^{-\delta}M^{+\delta})_n \rightleftarrows n\,A^{-\delta}M^{+\delta} \rightleftarrows A^{-}M^{+} \rightleftarrows A^{-} \| M^{+} \quad (11)$$
$$A^{-} + M^{+}$$

In glycol ethers and many cyclic ethers, the existence of the polar molecules $A^{-\delta}M^{+\delta}$ and their aggregates $(A^{-\delta}M^{+\delta})_n$ is atypical and two main types of ion pairs predominate, contact ion pairs ($A^{-}M^{+}$, c.i.p.) and separated ion pairs ($A^{-}\|M^{+}$, s.i.p.); on the other hand, the concentration of free ions (A^{-}, M^{+}) is low. The main difference between the separated and contact ion pairs is the presence of a layer of solvent molecules (usually the solvation shell of the cation) separating the ions, as a result of which the interionic interaction in a separated ion pair is of a Coulombic type and hardly depends on the radius of the cation.

In contact ion pairs, a decrease of the radius of the cation entails an appreciable enhancement of the interionic interaction and the exchange energy begins to play a decisive role in this process. The formation of separated ion pairs is favoured by an increase of the degree of solvation of the cation which may be a consequence of its reduced radius, the enhancement of the solvating capacity of the solvent, or a decrease of temperature. For large cations (K^{+}, Rb^{+}, and Cs^{+}), the existence of separated ion pairs in an ethereal medium is unlikely.

The different types of ion pairs are distinguished with the aid of many physicochemical methods—by the shift of the absorption band maximum in the spectrum of the carbanion; by the splitting of the components of the ESR spectrum as a result of the interaction of the unpaired electron with the magnetic moment of the nucleus of the cation; by the heat of dissociation of ion pairs, into free ions established by measuring the conductance of the solution as a function of temperature. Much information can be obtained also with the aid of the NMR method [47-50]. Contact ion pairs with unequal degrees of solvation of the cation may be distinguished spectroscopically [51] and by ESR [52] and it is also possible to detect the so called peripherally solvated [7,53] contact ion pairs which are isomeric with separated ion pairs. More detailed information about the state of organic compounds of alkali metals in solution is given in other reviews [5,7,13,49,53-56].

The extensive literature on the structure and properties of radical-anions and dianions and on the state of the adducts in solution has been summarised in other reviews [3-9,12,13]. The problem of the reactivities of radical-anions and dianions has been less thoroughly considered and general accounts of the information about their behaviour in metallation reactions, particularly as a function of the counterion, the properties of the solvent, and the type of ionic association complexes, are altogether lacking. The aim of the present review is to fill this gap. Since in the course of metallation reactions involving radical-anions and dianions the carbanions of dihydro-derivatives of aromatic hydrocarbons are formed, one of the sections of the review is devoted to the metallation of aliphatic-aromatic compounds by such species.

II. RADICAL-ANIONS AS METALLATING AGENTS

Normant and Angelo [16] were the first to note the possibility of using radical-anions for metallation. They showed that in THF sodionaphthalene, sodiobiphenyl, and

other adducts metallate in the CH bond aliphatic-aromatic hydrocarbons (fluorene, triphenylmethane, etc.), various derivatives of acetylene, nitriles, carboxylic acids, and certain heterocyclic compounds, both rapidly and in high yields. It has been established for the metallation of diphenylmethane that the naphthalene radical-anions are more effective than the phenanthrene radical-anions and that the rate of reaction increases when the sodium cation is replaced by potassium.

Table 1. Rate constants ($10^3 k$, litre mole^{-1} s^{-1}) for the reaction of radical-anions (K^+ cation) with triphenylmethane at 20°C.[57,58]

Radical-anion	DG	DME	DEE	DMP
Biphenyl	55	25	10	12
Napthalene	1.6	1.3	2	5
Anthracene	—	0.6	~0.1	—

Eisch and Kaska[18] observed that metallation with the aid of lithiobiphenyl in THF at 30°C is quantitative for triphenylmethane, takes place to the extent of 50% for diphenylmethane, and not more than 1% for toluene. The metallation reaction was accelerated by the addition of metallic lithium to lithiobiphenyl, which was explained by the formation of the biphenyl dianion more reactive than the radical-anion.

Table 2. Rate constants ($10^3 k$, litre mole^{-1} s^{-1}) for the reaction of radical-anions (Na^+ cation) with 9-phenylxanthene at 20°C.[58]

Radical-anion	DG	DEE
Biphenyl	16	200
Naphthalene	7	11

Later studies were made[57-60] on the dependence of the rate of metallation of certain aliphatic-aromatic compounds on the structure of the radical-anion, the substrate, and the cation on the solvating properties of the ether.

Usually the protophilic properties (or in the more general case the nucleophilic properties) of the carbanion become more pronounced as the interaction with the counterion weakens. This has been demonstrated in numerous instances of anionic polymerisation reactions[7,61], metallation by organolithium compounds[54], hydrogen isotope exchange between the CH bonds of two hydrocarbons in catalysis by bases[62], etc. The same cause is responsible for the acceleration of the majority of anionic organic reactions in solvents which effectively solvate cations and thereby activate the anions[5,63-65].

However, Tables 1 and 2 show that the effect of interionic interaction in metallation reactions involving radical-anions does not always obey the above rule and is related in a specific manner to the structure of the reactants.

Thus, in the reaction with triphenylmethane, the protophilic properties of the biphenyl radical-anion become more pronounced on passing from 1,3-dimethoxypropane (DMP) and 1,2-diethoxyethane (DEE) to solvents with a higher solvating capacity[5]—[1,2-dimethoxyethane?(Ed. of Translation)] (DME) and diglyme (DG) (Table 1). At the same time the opposite variation of the effect of the medium on the rate of reaction has been observed for the naphthalene radical-anion under the same conditions, i.e. an unusual behaviour has been observed, the protophilic properties of the radical-anion proving to be more marked the more intense its interaction with the cation. In the metallation of 9-phenylxanthene by sodium adducts the same behaviour is shown also by the biphenyl radical-anion (Table 2). It has been demonstrated[58] that the biphenyl and naphthalene radical-anions form with the Na^+ cation separated ion pairs in DG and contact ion pairs in DEE, i.e. contrary to the usual belief, the reactivity of the separated ion pairs is inferior to that of the contact ion pairs.

Table 3. Rate constants ($10^4 k$, s^{-1}) for the reaction of naphthalene radical-anions with triphenylmethane at 22°C.[57]

Solvent	Na^+	Li^+	K^+	Cs^+
DME	0.5	1	1	>10
DEE	0.8	1.2	2.5	>10

Essentially the same conclusion can be reached also on the basis of data for the effect of the cation on the rate of metallation of triphenylmethane by the naphthalene radical-anion in DME and DEE (Table 3). In DME, sodionaphthalene is present predominantly in the form of separated ion pairs and potassionaphthalene and caesionaphthalene are mainly in the form of contact ion pairs[5], but the rate of metallation is in fact higher for the contact ion pairs.

The above findings suggest that the cation enters into the composition of the activated complex for the reactions involving the metallation of aliphatic-aromatic compounds with participation of radical-anions.

An unusual dependence of the protophilic properties of the radical-anion on the intensity of interionic interaction has been observed also in certain other reactions with an acid-base mechanism. Thus weaker protophilic properties of the radical-anions entering into the composition of the separated ion pairs compared with the contact ion pairs were noted by Bank, who measured the rate of reaction of sodionaphthalene[38] and sodioanthracene[34] with water (Table 4).

For example, when tetraglyme (0.01% in relation to sodionaphthalene) is added to THF, the sodionaphthalene contact ion pairs are converted into separated ion pairs[7,53] and the rate of reaction with water then decreases by two powers of ten. The addition of tetraglyme (13 mole %) to THF causes a similar decrease (by a factor of 110) of the rate of protonation of the anthracene radical-anion. The type of dependence of k_1 and k_2 on the solvent is not altogether the same (cf. k_1 and k_2 for THF + DME and DME in Table 4). Bank and Bockrath attribute this to differences in the structure of the transition states[34].

Smid[49,55] showed that, when 1,4-dioxan (DO) is replaced by THF, the interionic interaction in the fluorenylsodium contact ion pairs is weakened. The protophilic

properties of the fluorene carbanion should then become more marked; however, measurements of the rate of reaction of fluorenylsodium with 1,2-benzofluorene [66] (Table 5) have shown that the protophilic properties of this anion become weaker. The addition of tetraglyme to THF causes the formation of separated ion pairs as for sodionaphthalene, but the rate of transfer of the proton to fluorenylsodium decreases by a factor of six, whereas in DME the formation of separated ion pairs is accompanied, as usual, by an enhancement of the protophilic properties of the carbanion.

Table 4. Rate constants (k, litre mole^{-1} s^{-1}) for the reactions of sodionaphthalene [33] (k_1) and sodioanthracene [34] (k_2) with water at 20°C.

Solvent	$10^{-4}k_1$	$10^{-4}k_2$
THF	1.06	0.66
THF + DME (50 vol.%)	0.79	0.013
DME	0.31	0.017
THF + tetraglyme	0.023	0.006

In a study of the kinetics of the isotope exchange of molecular deuterium with the adduct of an alkali metal and benzonitrile, Japanese workers [67] established that the rate of reaction increases with the radius of the cation in the adduct and on weakening of the solvating capacity of the solvent (Table 6).

Table 5. Rate constants (k, litre mole^{-1} s^{-1}) for the reactions of fluorenylsodium with 1,2-benzofluorene at 25°C. [66]

Solvent	Type of ion pair	$10^{-3}k$
DO	c.i.p.	4.2
THF	c.i.p.	3.5
THF + tetraglyme	s.i.p.	0.6
DME	s.i.p.	50

Consequently in this case the enhancement of the interionic interaction of the radical-anion with the counterion tends to increase the reactivity of the adduct (see Refs. 68–70 for other studies on these lines).

All that has been said concerning the anomalous dependence of the protophilic properties of the radical-anions and carbanions on the intensity of the interaction with the cations suggests that the cation can play a significant role in the transition state of the rate-limiting step of the proton transfer process. In particular, the observed effects can be accounted for if it is assumed [33,34,58,66] that the cation activates the bond which functions as the proton donor. An increase of the cation radius and a decrease of the solvating capacity of the solvent are accompanied by a decrease of the degree of solvation of the cation, which should entail an increase of the electrophilic properties of the latter. This leads to an acceleration of the reaction, in agreement with experimental results. The idea of an electrophilic attack by the cation on the CH bond of the substrate is not new—it was put forward and defended long ago by Morton [71]. Experimental data failed to confirm this hypothesis for reactions involving the substitution of hydrogen by a metal under the action of strong bases and it was justly criticised [72]. However, in relation to protonation reactions of radical-anions, the idea is supported by data for the kinetic isotope effect (KIE).

Table 6. Rate constants (k, ml h^{-1}) for isotope exchange between D_2 and the benzonitrile radical-anion [68].

Cation	Solvent	k	Cation	Solvent	k
Li$^+$	THF	0.1	K$^+$	DME	2.0
Na$^+$	THF	4.8	K$^+$	DG	0.58
K$^+$	THF	10.0	K$^+$	triglyme	0.32

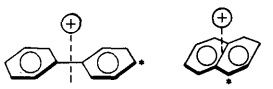
Usually, in metallation reactions involving a protophilic hydrogen substitution mechanism, the rate-limiting stage is the dissociation of CH bonds [72]. In this case a high KIE is observed [73]. For example, a KIE close to the maximum possible value $k_H/k_D = 10$ has been observed [74] for the metallation of triphenylmethane by n-butyl-lithium in ethyl ether and THF. However, in reactions of potassiobiphenyl and potassionaphthalene with triphenylmethane in DEE [58] at 25°C, the ratio $k_H/k_D \simeq 1$. A low value of KIE was also established by Bank in the reaction of sodionaphthalene ($k_H/k_D = 1.37 \pm 0.44$) [33] and sodioanthracene ($k_H/k_D = 2.02 \pm 0.68$) [34] with water in THF at 20°C. The author adopted the concept of the involvement of the counterion in the transition state of the protonation reaction and emphasised that it remains important in the interaction of the radical-anion with acids such as triphenylmethane, and water which differ greatly in acid strength.

According to Melander [73], a low KIE should be observed in reactions where the electrophilic attack by the cation precedes or takes place simultaneously with the dissociation of the CH bond. This has in fact been established [33,34,58].

The reason why the cation must be involved in the proton transfer process may be the considerable degree of delocalisation of the charge in the radical-anions of aromatic hydrocarbons [3,13]. Therefore the electron density at the reaction centre of the radical-anion is low and its protophilic properties are comparatively weak. The available literature data for KIE in metallation reactions suggest that the degree of involvement of the cation in the transition state increases with decrease of the protophilic properties of the carbanion. For example, in the metallation of triphenylmethane by organolithium compounds in THF, [75] a tendency was observed towards a decrease of the k_H/k_D ratio on decrease of the basicity of the anion (alkyl > phenyl > benzyl) of the metallating agent. According to West et al. [75], the lithium cation is involved in the transition state, the degree of its involvement increasing on passing to less basic carbanions. However, under these conditions the dissociation of the CH bond remains the rate-limiting stage of the reaction ($k_H/k_D \simeq 9-4$).

On the other hand, one cannot restrict the role of the cation to electrophilic attack alone. In our view, one cannot rule out the possibility that the change of electron

density distribution, caused by the cation, in the radical-anion in the transition state, giving an increased electron density at the reaction centre, is also important. Then, if the cation is near the reaction centre, a decrease of the degree of its solvation and the increase of electrophilicity will promote such redistribution (the dissociation of the CH bond will probably not be [will probably be?] the rate-limiting stage, as before). On the other hand, if the cation and the reaction centre are far from one another, the decrease of the degree of solvation of the cation may retard the reaction. When the location of the cation in relation to the radical-anion is symmetrical, the reaction centre (designated by an asterisk) in the biphenyl radical-anion is further away from the cation than in the naphthalene radical-anion. This difference may be the reason for the opposite influence of solvents on the reactivity of potassiobiphenyl and potassionaphthalene:



On the other hand, if one remembers that the cation can fulfill a dual function—that of an electrophilic agent in relation to the CH bond and of a polarising agent in relation to the radical-anion—it becomes evident that the dependence of the rate of reaction with the given substrate on the structure of the radical-anion, the size of the cation, and the solvating capacity of the solvent may become complicated and difficult to predict.

Thus the study of the reactions of various proton donors with radical-anions led to the formulation of many new hypotheses concerning the relation between the state in solution and the reactivity of adducts of alkali metals and aromatic hydrocarbons. Similar phenomena have been observed also for the radical-anions of aliphatic-aromatic hydrocarbons formed in the reactions of the latter with alkali metals.

III. RADICAL-ANIONS IN REACTIONS OF ALIPHATIC-AROMATIC COMPOUNDS WITH ALKALI METALS

The interaction of alkali metals with various compounds containing a CH bond in which the hydrogen atom is mobile entails [1,72] the substitution of the latter by the metal. Liquid ammonia [37,76,77], in which alkali metals readily dissolve, and other electron-donating solvents, for example THF, [78] are convenient media for reactions of this kind. The effectiveness of these solvents is due to the solvation of the alkali metal cation, which facilitates the conversion of the metal atom into an ionised form. This conclusion follows, in particular, from the studies of Scherf and Brown [79,80], who showed that the reaction of fluorene with lithium, sodium, and potassium becomes easier in a sequence corresponding to the solvating capacity of the ethers [5,62]: DME > THF ≥ DEE > DO.

It was suggested initially that the reaction has an acid–base mechanism [72] with dissociation of the CH bond and ionisation of the metal atom in a single elementary step (here and henceforth the aliphatic-aromatic compound will be denoted by AH in contrast to the purely aromatic compound Ar):

$$AH + M \rightarrow A^{-\delta}M^{+\delta} + H^{\bullet}\,. \qquad (12)$$

The evolution of hydrogen, quoted by a number of workers [77-79], in the reactions of hydrocarbons with alkali metals is at first sight consistent with this view. However, later investigations [18,81,82] suggested that the reaction may be more complicated—it may proceed via a one-electron transfer stage with formation of a radical-anion $AH^{\bullet-}$:

$$AH + M \rightleftharpoons AH^{\bullet-} + M^{+}\,. \qquad (13)$$

The first ESR studies [83,84] already confirmed the formation of the radical-anions of aliphatic-aromatic hydrocarbons in their interaction with alkali metals in an ethereal medium. Comparatively stable (as a rule at low temperatures) radical-anions of indene [83], fluorene [83-86] and its derivatives [87-89], isomeric benzofluorenes [84,90], and 4,5-methylenephenanthrene [84,90-92] were obtained.

The mode of further reactions of the radical-anions in many ways depends on the structure of the hydrocarbon. Thus the radical-anions of arylmethanes mainly undergo the dissociation of the C–C bond with elimination of the benzene ring [81, 93-95]. The conversion of the radical-anion into a metallation product (the carbanion A^{-}) with dissociation of the CH bond and elimination of a hydrogen atom is possible [93-96]:

$$AH^{\bullet-} \rightarrow A^{-} + H^{\bullet}\,. \qquad (14)$$

Reaction (14) is more typical for the radical-anions of indene, fluorene, and similar compounds [82-84,97-98]. Hydrogen is evolved in a gaseous form and is consumed in the hydrogenation of the radical-anion,

$$AH^{\bullet-} + H^{\bullet} \rightarrow AH_2^{-} \qquad (15)$$

or of the initial hydrocarbon AH, or it remains in solution [83,84]:

$$AH + H^{\bullet} \rightarrow AH_2^{\bullet} \qquad (16)$$

and

$$AH_2^{\bullet} + AH^{\bullet-} \rightarrow AH_2^{-} + AH\,. \qquad (17)$$

When the reaction mixture contains sufficient of the initial compound AH, the latter may react with the radical-anions in accordance with Eqns. (18) and (19): [18,82-84]

$$AH^{\bullet-} + AH \rightarrow AH_2^{\bullet} + A^{-}\,, \qquad (18)$$

$$AH_2^{\bullet} + AH^{\bullet-} \rightarrow AH_2^{-} + AH\,. \qquad (19)$$

Eqns. (18) and (19) are analogous to Eqns. (1) and (2), AH playing the role of the proton donor BH in relation to its own radical-anions. The AH_2^{-} carbanions are usually more basic than A^{-} and are protonated by the initial hydrocarbon with formation of the dihydro-derivative AH_3:

$$AH_2^{-} + AH \rightarrow AH_3 + A^{-}\,. \qquad (20)$$

Thus the mechanism of the reaction in a system containing an aliphatic-aromatic hydrocarbon and an alkali metal is very complicated. One should note that the metal cation, the role of which in the process may be very considerable, as already demonstrated above, has been omitted from the equations.

It is usually almost impossible to obtain an unambiguous idea about the mechanism on the basis of kinetic data determined by any one method (for example from measurements of the electronic and ESR spectra and from the amount of hydrogen evolved). It is also difficult because all three modes of reaction of AH^{-} [reactions (14) and (15), (14)–(17), and (18)–(19)] are equivalent from the standpoint of the final result (the formation of the carbanions AH_2^{-} and A^{-}) and can be formally represented by the same overall equation for the disproportionation of two radical-anions:

$$AH^{\bullet-} + AH^{\bullet-} \rightarrow AH_2^{-} + A^{-}\,. \qquad (21)$$

The detection of AH_3 among the reaction products indicates the involvement of the initial AH in the reactions of the radical-anion but it is not clear in what capacity—as a hydrogen atom acceptor [Eqn.(16)] or as a proton donor [Eqn.(18)]. Nevertheless, it is important to know this also from the point of view of the characteristics of the reactivity of the radical-anion, which in the first case behaves only as an electron donor [Eqn.(17)] and in the second as a proton acceptor [Eqn.(18)]. In the determination of the activation parameters for the decomposition of $AH^{\cdot-}$, it is difficult to rule out the presence of AH, since equilibrium (13) shifts to the left with increase of temperature. However, even when the hydrocarbon AH is not present in solution, the possibility of the consumption of the radical-anion via two pathways [reactions (14) and (15)] remains. Taking this into account, we shall examine the available literature data for the effect of the metal and solvent on the course of the reaction involving the metallation of aliphatic-aromatic hydrocarbons by alkali metals.

Scherf and Brown [79] showed that the effectiveness of alkali metals in the reaction with fluorene decreases in the sequence K > Li > Na. The rate of conversion of fluorene radical-anions into carbanions, measured [83] by the ESR method in DME, decreases in the same sequence.

Since the kinetic data [79,83] characterise the overall reaction of the radical-anion [Eqns.(14)–(19)], it is difficult to derive from them a clear idea about the effect of the cation on the behaviour and reactivity of the radical-anion.

The results obtained by Tabner, who made a detailed investigation of the kinetics of the conversion of the radical-anions of fluorene [86] and its derivatives [88–90] into the corresponding carbanions, suffer from the same deficiency. The kinetic parameters were determined in a system containing the radical-anions prepared at a low temperature (−80°C) in the presence of an excess of the alkali metal. Therefore it was postulated that the free hydrocarbon is absent from the solution and reactions (16)–(19) were excluded from consideration *a priori*. Nevertheless, a certain amount of AH might have formed in the system on raising the temperature in consequence of a shift of equilibrium (13). Moreover, the rate of evolution of hydrogen was not determined and the conclusions concerning the mechanism and the role of the cation in it were reached on the basis of kinetic data obtained spectrophotometrically or by the ESR method. In view of this, a detailed analysis of Tabner's data is pointless, and we shall consider only the most important results.

Table 7 presents the free energies of activation ($\Delta G^{\neq}$, kcal mole^{-1}) for the conversion of the fluorene radical-anions into carbanions, the temperature ranges (t_1 and t_2, °C) in which the rate constants k were measured, the values of k corresponding to the extreme temperatures (k_1 and k_2), and the order of the reaction n with respect to the radical-anions.

It is difficult to infer the effect of the cation from the rate constants, since the measurements were made in different temperature ranges. Sometimes the k cannot be compared as they have different dimensions. Since the rate decreases as the temperature is reduced, it follows, judging from the value of k with the same dimensions, that the dependence of the rate of reaction in THF on the cation is represented by the following sequence: $Li^+ < Na^+ < K^+ < Cs^+$. In the case of Cs^+, the rate of reaction was so high that it could not be measured. The activation energy for the first-order reaction in THF also decreases with the radius of the cation. Tabner's results differ from the data of Scherf and Brown [79] and Bilevich et al. [83] by the position of lithium in the series of cations. Possibly this is due to the difference between the solvents and temperatures. The effect of the cation depends also on the structure of the hydrocarbon. Thus the rate of decomposition of the 1,2- and 2,3-benzofluorene radical-anions [90], obtained by the reaction with sodium, is higher than that of the radical-anions obtained by the reaction with lithium, while for 4,5-methylenephenanthrene the most stable radical-anions were in fact obtained in THF by the reaction with sodium.

Table 7. Effect of the cation and the solvent on the kinetics of the conversion of the fluorene radical-anions into carbanions [8].

Cation	Solvent	t_1,°C	t_2,°C	$k_1\cdot10^3$	$k_2\cdot10^3$	n	$\Delta G^{\neq}_{25}$
Li^+	THF	+9.4	−6.1	1.2	0.415	1	20.8
Li^+	THF	−20.2	−37.5	60.2*	21.3*	2	17.9
Na^+	THF	−30.7	−41.2	1.6	0.46	1	18.1
K^+	THF	−38.7	−53.2	25	1.8	1	14.8
Li^+	DME	−18	−43.3	25.8*	0.24*	2	16.9
Li^+	THP**	−17.8	−48.4	9.95	0.39	1	18.3
Li^+	MTHF**	−23.2	−43.4	10.1	0.66	1	13.8

*The dimensions of the constants are litre mole^{-1} s^{-1}; in the remaining cases the dimensions are s^{-1}.
**THP = tetrahydropyran; MTHF = 2-methyltetrahydrofuran.

Tabner observed that the reaction may be of first or second order with respect to the radical-anion [86] (Table 7). Analysis of the conditions under which the reaction was carried out led him to the conclusion that a first-order reaction is observed for contact ion pairs and a second-order reaction for separated ion pairs. Admittedly the type of ion pairs was not identified, but Tabner's conclusion appears likely, since a second-order reaction was observed either at low temperatures (in THF) or in solvents with a relatively high solvating capacity (DME). In addition, a second-order reaction with respect to the radical-anion was observed also for isomeric benzofluorenes [90], where an appreciable delocalisation of the charge also favours the formation of separated ion pairs.

The second-order reaction may be a consequence of the fact that the transition state of the rate-limiting stage [it is believed that this is reaction (14)] has the structure of a contact ion pair, i.e. the cation is actively involved in its formation. In relation to the free radical-anion or the radical-anion forming part of the separated ion pair, the cation behaves in this case like a kinetically independent species, which leads to a second-order reaction.

The authors believe that the role of the cation consists in the localisation of the negative charge near the carbon atom of the CH aliphatic bond [86], which is favoured by the intense interionic interaction in contact ion pairs. The necessity to localise the charge near the reaction centre is believed to be due to the fact that the structure of the transition state is closer to that of the reaction product (the anion A^-) then to the initial radical-anion [90]. In particular, this is indicated by the correlation between the acidity of the hydrocarbons and the rate of decomposition of their radical-anions (Table 8).

The decrease of the solvation energy of the cation, tending to increase its electrophilicity, should probably enhance the localisation of the charge by the cation.

Possibly this is one of the reasons for the acceleration of the decomposition of the radical-anion with increase of the radius of the cation, since the greater its radius the lower the degree of its solvation. We may note that, on passing from diglyme to dioxan, the degree of solvation of the cation falls and the rate of evolution of hydrogen in the reaction of cyclopentadiene with potassium rises [97].

Table 8. The acidity of the hydrocarbons (pK) [99] and the relative rate constants (lg k_{rel}) for the decomposition of their radical-anions (Li^+ cation) in THF at 25 °C. [90]

Hydrocarbon	pK	lg k_{rel}
1,2-Benzofluorene	20.0	0.91
4,5-Methylenephenanthrene	22.6	0.51
Fluorene	22.9	0.00
2,3-Benzofluorene	23.2	—1.67

Nevertheless, it would be premature to assume that there is a fully unambiguous relation between the type of ion pairs and the effect of the cation in the conversion of the radical-anions of aliphatic-aromatic hydrocarbons into carbanions. There are facts which are difficult to account for within the framework of the above hypothesis concerning the structure of the transition states; these include, in particular, data [86,89,90] indicating a dependence of the activation parameters for the reaction on the cation and on the solvent. Possibly this difficulty will be overcome after more detailed studies of the decomposition of the radical-anion.

The increased probability of decomposition of the radical-anion involving dissociation of the CH bond via reaction (14) with increase of the acidity of the hydrocarbon was noted not only by Tabner [86] but also by other workers. Bosch and Brown [82] established that, when indene is metallated by potassium and lithium in DME at 85 °C, a much greater amount of hydrogen is evolved than in the metallation of a less acid hydrocarbon—fluorene (50–60% and 2–14% of theoretical respectively). It has also been noted [83] that the fluorene radical-anion is more stable than the indene radical-anion. On the other hand, it is evident that an increase of acidity tends to accelerate the protonation of the radical-anion [reaction (18)], which competes with reaction (14). Since the kinetics of both processes depend in a complex manner on the cation, the solvent, and the structure of the radical-anion, it follows that the relative contributions of reactions (18) and (14) can vary in different ways depending on the specific experimental conditions. This is confirmed by measurements [98] of the rate of metallation of the same hydrocarbons by potassium in THF at 25 °C (Table 9).

Probably not only the acidity of the hydrocarbon but also its structure as a whole has a significant influence. It has been suggested [84] that, for a fairly high degree of delocalisation of the unpaired electron (for example in the ring fragment of the naphthyl or phenanthryl ion), the radical-anions of fairly acid hydrocarbons can also be stable. For example, the radical-anion of 4,5-methylenephenanthrene [92] (pK = 22.6) is stable at room temperature.

In conclusion of this section, we shall mention yet another reaction which may occur in a system containing an aliphatic-aromatic hydrocarbon and an alkali metal. In the presence of an excess of the latter, the anions A^- may, like those of aromatic hydrocarbons, combine with a further electron and give rise to radical-dianions (r.d.a.):

$$A^- + M \rightarrow A^{=} + M^+ . \qquad (22)$$

One of the first radical-dianions of this kind was detected in the reaction of cycloheptatriene with potassium in RHF. [100,101] However, radical-dianions were in fact obtained even earlier. Thus it has been noted [80] that the reaction of a second equivalent of potassium with fluorenylpotassium proceeds without the evolution of hydrogen. The authors could not account for this phenomenon, since they assumed that the second hydrogen atom in the 9-position must be substituted by the metal. It was not until later that Janzen and Gerlock [84] showed with the aid of ESR that the addition of a second potassium atom with formation of a radical-dianion takes place under these conditions and not substitution. Syrkin and coworkers [102] observed the formation of radical dianions in the polarographic reduction of aromatic compounds in DMF. So far, the radical-dianions of fluorene [84,103], 9-phenylfluorene [87,103,104], benzofluorenes [87,103], and diphenylmethane [95] have been identified by ESR; the ESR spectra of 4,5-methylenephenanthrene have been investigated in greatest detail [84,92,103–105].

Table 9. The acidity of the hydrocarbons (pK) [66] and the rate constants (k, s^{-1}) for the evolution of hydrogen in the course of their metallation by potassium in THF at 25 °C. [98]

Hydrocarbon	pK	$k \cdot 10^8$
Cyclopentadiene	15—17	1.0
Indene	21	1.5
Fluorene	25	1.9

Usually radical-dianions are formed readily when hydrocarbons are metallated by potassium and the reaction can proceed even in the melt in the absence of a solvent [95]. With sodium, it is not always possible to obtain radical-dianions even for hydrocarbons with an extensive π-conjugation system, such as benzofluorenes. From the standpoint of reactivity, the radical-dianions have been hardly investigated; it has only been stated that they may be protonated by the solvent (DME). [92] There is no doubt that the study of the chemical behaviour of these species, which combine properties of a radical-anion and a dianion, can yield very interesting and useful results.

IV. DIANIONS AS METALLATING AGENTS

The dianions of aromatic hydrocarbons are stronger bases than the radical-anions. For example, the metallation of triphenylmethane by the dianions of naphthalene [106], biphenyl [107], and anthracene [57] is faster by several powers of ten than the metallation by radical-anions under the same conditions. The high reactivity of the dianions is to some extent an obstacle to its quantitative investigation. The protophilic properties of the dianions are so marked that they are protonated by the solvent and not only by fairly acid solvents such as ammonia [108] but also by much

weaker proton donors—ethers. Thus dilithionaphthalene cannot be obtained in an ethereal medium without admixture with an organic derivative of the alkali metal the absorption spectrum of which resembles that of the dihydronaphthalene carbanion [5,109,110]. It has been shown [106,111] that the diphenyl and anthracene dianions, obtained by the reduction of the corresponding radical-anions with potassium or lithium in DME and DEE, are converted after a time, in a solution free from acid impurities, into carbanions the spectroscopic properties of which resemble the carbanions of dihydro-derivatives.

It has recently been shown [112] that the protonation of the dianions by the solvent is the reason for the earlier observation [57] of the conversion of the naphthalene radical-anions into the carbanions of the above type in the presence of an excess of the alkali metal. This process is faster the lower the ionisation potential of the metal and the higher the solvation capacity of the solvent. In other words, this reaction is promoted by the same factors as those favouring the formation of the dianions [5]. Szwarc and coworkers showed that the protonation of the diphenylacetylene [113] and methylphenylacetylene [31] dianions in THF causes in the course of time a shift of the equilibrium in the reaction of these hydrocarbons with sodionaphthalene or sodiobiphenyl. A slow protonation of the naphthalene dianions by ethers (DO and THF) has been reported [28].

The low stability of solutions of the dianions hinders the study of the effect of the cation and the solvent on the reactivity of the dianions. One-electron transitions, which are more likely than in the case of radical-anions, give rise to an additional complication. For example, the interaction of the anthracene dianion with 2-methylnaphthalene leads to the formation of the carbanion of the latter. However, the naphthalene and biphenyl dianions convert 2-methylnaphthalene into radical-anions, while metallation does not take place [106].

Table 10. Rate constants (k, s^{-1}) for the reaction of diphenylmethane with anthracene dianions and the positions of the maxima (λ_{max}, nm) in the spectra of the dianions [106].

Cation	Solvent	k	λ_{max}
Li^+	DEE	$\gg 10^{-7}$	565
Na^+	DEE	$\sim 10^{-7}$	590
K^+	DEE	$2 \cdot 10^{-3}$	615
Na^+	DME	$1 \cdot 10^{-4}$	600
K^+	DME	$>10^{-3}$	615

The effects of the cation and the solvent on the reactivity of the dianion obey the usual relations governing the protophilic substitution of hydrogen, i.e. the reaction rate increases as the interaction between the dianions and the counterions is weakened. For example, the rate of reaction of the naphthalene dianion with diphenylmethane in THF ($k \simeq 10^{-2}$ s^{-1}) is much higher than in DEE ($k = 6 \times 10^{-4}$ s^{-1}), [106] where the lithium cation is less solvated. The interaction of the anthracene dianion with the cation becomes weaker with increase of the radius of the latter in the series $K^+ > Na^+ > Li^+$ or when the solvating capacity of the solvent is impaired (DME > DEE), as shown by the bathochromic shift of the absorption band in the spectrum of the anthracene dianion [111]. The rate of reaction of the anthracene dianion with diphenylmethane also increases in the same direction [106] (Table 10).

Apparently the protophilic properties of the dianion are fairly marked and there is no need for the activation of the metallated linkage by the cation or for the increase of the electron density at the dianion reaction centre in the transition state, as suggested for radical-anions. In this connection, it is interesting to note that a high KIE ($k_H/k_D \simeq 10$) [35] has been found for the reaction of the perylene dianion with alcohol in THF, as for metallation by lithium alkyls [74,75].

On the other hand, the problem of the effect of the cation on the reactivity of the dianion cannot be regarded as finely elucidated. According to the date of Ichikawa and Tamaru [114], the rate of isotope exchange of D_2 with anthracene dianions (it is assumed that the exchange involves an acid–base mechanism) increases when Li^+ and Na^+ cations are replaced by cations with a larger radius, in agreement with results [106] obtained in a study of metallation reactions. On the other hand, the adsorption of hydrogen in solutions of the dianions, leading to the formation of the carbanions of dihydroanthracene and the alkali metal hydride [70], is faster for cations with small radii [114].

V. CARBANIONS OF DIHYDRO-DERIVATIVES OF AROMATIC HYDROCARBONS AS METALLATING AGENTS

On reaction with proton donors, the radical-anions and dianions of aromatic hydrocarbons are converted into the carbanions of the dihydro-derivatives [mechanisms (1), (2), and (4)]. Until recently, special attention was not paid to the behaviour of these carbanions in the metallation or Birch reduction reactions and yet the final result of the process depends on them in many ways. For example, it has been shown [108] that, in the reductive alkylation of biphenyl in liquid ammonia, the species involved in the reaction with methyl bromide is not the biphenyl dianion formed in the first stage but its protonation product—the carbanion of dihydrobiphenyl.

In DME and DEE, the carbanions of dihydrobiphenyl are less protophilic than the biphenyl radical-anions, whereas in diglyme as a solvent, which has a higher solvating capacity, the opposite relation between their reactivities is obtained [106]. Therefore the metallation of triphenylmethane and 9-phenylxanthene in DME or DEE is complicated by the accumulation of dihydrobiphenyl carbanions in solution. In particular, the metallation of 9-phenylxanthene by sodiobiphenyl in DEE is on the whole slower for this reason than in diglyme, despite the fact that the rate of reaction of the biphenyl radical-anion with this substance in DEE is much higher than in diglyme (Table 11).

In general, in solvents with a comparatively low solvating capacity the rate of metallation directly by the radical-anion or dianion of biphenyl is ultimately determined by the reactivity of the dihydrobiphenyl carbanions [58,106,107]. At the same time, in all the instances where the reactions of aliphatic-aromatic compounds with the carbanions of dihydronaphthalene and dihydroanthracene were investigated, the reactions are faster than those with the corresponding radical-anions but slower than with the dianions [57,106]. Thus smaller rate constants have been obtained for the metallation of diphenylmethane by dihydronaphthalene carbanions [106] (with Li^+ cations), $k = 2.3 \times 10^{-5}$ s^{-1} in THF and 2.5×10^{-4} s^{-1} in DEE, than for the

naphthalene dianions (9.5×10^{-3} and 6×10^{-4} s^{-1} respectively). The higher reactivity of the dihydroanthracene carbanion compared with the anthracene radical-anion in protonation by water has also been noted [34]. It was explained by the fact that the electron density in the 9-position of the radical-anion is smaller by a factor of two than in the carbanions. Deuterium exchange with dihydroanthracene carbanions [114] is slower than with anthracene dianions, which also indicates more marked protophilic properties of the latter. As far as one can judge from the data in Table 11, an increase of the degree of solvation of the cation tends to increase the protophilic properties of the carbanions of the dihydro-derivatives.

Table 11. Rate constants for the metallation (litre $mole^{-1}$ s^{-1}) of triphenylmethane and 9-phenylxanthene by biphenyl radical-anions (k_1) and dihydrobiphenyl carbanions (k_2). [106]

Hydrocarbon	Cation	Solvent	$k_1 \cdot 10^3$	$k_2 \cdot 10^3$
Triphenylmethane	K^+	DG	55	>1000
"	K^+	DME	25	11
"	K^+	DEE	10	5
9-Phenylxanthene	Na^+	DG	16	>1000
"	Na^+	DEE	200	11

As already stated (Section I), the position of equilibrium in the reactions of such carbanions with aliphatic-aromatic compounds is determined primarily by the strength of the CH acids involved in them. Dihydrobiphenyl and dihydronaphthalene are apparently very weak CH acids ($pK > 33$), while the equilibrium acidity of dihydroanthracene, determined in cyclohexylamine [115] by the transmetallation method, is somewhat higher than that of triphenylmethane [116] (the respective pK values are 30.4 and 31.5).

Table 12. Equilibrium constants for the reactions of dihydroanthracene carbanions with triphenylmethane at 25°C. [115]

Cation	Solvent				
	DG	DME	DEE	DE*	CHA*
Li^+	2.3	2.8	44	125	—
Na^+	—	3.0	17	—	—
K^+	3.0	4.8	17	30	12
Cs^+	5.1	11	11	—	12

*DE = diethyl ether; CHA = cyclohexylamine.

Therefore the reactions of the anthracene radical-anions or dianions with triphenylmethane [57,106] do not go to completion and equilibrium is established in the last stage. Its position depends significantly on the cation and solvent [115] (Table 12). The observed effects have been explained by the unequal changes in the energy of the interaction of dihydroanthracene and triphenylmethane carbanions when the reaction conditions are varied, in particular by a difference in the type of ion pairs in many instances.

It is noteworthy that the elucidation of the factors governing the influence of the structure of the ion pairs of organic derivatives of alkali metals on the position of the acid–base equilibrium of the transmetallation reaction is important for the problem of estimating the strength of CH acids by the above procedure [115,117-120].

VI. COMPARISON OF THE PROTOPHILIC PROPERTIES OF METALLATING AGENTS

The combined data for the reactivities of the above three types of metallating agents lead to the conclusion that the dianions are the most protophilic among them. The carbanions of the dihydro-derivatives are less reactive. The naphthalene and anthracene radical-anions are less protophilic than the carbanions, while the biphenyl radical-anions can be more protophilic than the carbanions of dihydrobiphenyl under conditions where the degree of solvation of the cation is comparatively low. The relative reactivities of the dianions, radical-anions, and the carbanions of dihydro-derivatives established in the metallation reactions are consistent with quantum-chemical predictions, in particular with calculations by the Pariser–Parr–Pople (PPP) method of the proton localisation energies [106] (Table 13).

Table 13. Protonation localisation energies for the dianions (L_1) and radical-anions (L_2) of aromatic hydrocarbons and the carbanions of their dihydro-derivatives (L_3) (in eV). [106]

Hydrocarbon	L_1	L_2	L_3
Biphenyl	0.34	—4.6	—5.1
Naphthalene	1.4	—5.2	—4.2
Anthracene	0.3	—5.4	—4.5

The protonation of the dianions entails an energy gain by the π-electron system, while the protonation of the radical-anions and the carbanions of the dihydro-derivatives is accompanied by a decrease of the π-conjugation energy. This implies that the dianions must be more protophilic than the other two types of agents, as in fact has been observed experimentally. Also in agreement with experiment, theory predicts a higher reactivity of the dihydronaphthalene and dihydroanthracene carbanions than that of the corresponding radical-anions ($L_3 > L_2$). On the other hand, according to theory, the protophilic properties of the biphenyl radical-anions should be more marked than those of the dihydro-biphenyl carbanions ($L_3 < L_2$). The opposite relation between the protophilic properties of the above two species observed in many cases is due to the effects of the medium and the counterions, which are so far difficult to take into account quantitatively in quantum-chemical calculations.

The absence of a correlation between the rate constant k for the protonation by water of the radical-anions of aromatic hydrocarbons and the localisation energies ($L_{r.a.}$) calculated for the protonation of the radical-anions by the simple Hückel method (Table 14) has been noted [30]. It is assumed that $L_{r.a.} = L + m_{m+1}$, where L is the localisation energy for the hydrocarbon and m_{m+1} the energy of

the lowest non-bonding hydrocarbon orbital in β units. For example, the rate of reaction falls on passing from the biphenyl to the anthracene radical-anion, despite the decrease of $L_{r.a.}$. At the same time, the authors noted a satisfactory agreement between the values of k and $L + 2m_{m+1}$ (or, what amounts to the same thing, between k and the sum $L_{r.a.} + m_{m+1}$). In their view, this is evidence that charge transfer from the radical-anion to the proton-donor molecule plays an important role in the mechanism of the protonation of the radical-anions (m_{m+1} characterises the electron affinity of the hydrocarbon and hence also the ionisation potential of the radical-anion).

Table 14. Rate constants for the protonation by water (k, litre mole^{-1} s^{-1}) of the radical-anions of aromatic-hydrocarbons and the localisation energies L calculated by the simple LCAO-MO method [30].

Hydrocarbon	$k \cdot 10^3$	L	$-m_{m+1}$	$L_{r.a}$	$L+2m_{m+1}$
Biphenyl	18	2.447	0.705	1.742	1.037
Naphthalene	4.6	2.299	0.618	1.681	1.063
Phenanthrene	1.0	2.299	0.605	1.694	1.089
Anthracene	0.2	2.015	0.414	1.599	1.185
1,2-Benzanthracene	0.055	2.049	0.452	1.597	1.145
Pyrene	0.012	2.190	0.445	1.745	1.300

Moreover, calculation by the more sophisticated PPP method yields values of $L_{r.a.}$ (Terekhova et al.[106]), the variation of which in the series of hydrocarbons (L_2 in Table 13) is consistent with the variation of the rates of the metallation (Tables 1 and 2) and protonation (Tables 4 and 14) [30,57,58] reactions. We may also note that the sum $L + 2m_{m+1}$ essentially defines the localisation energy for the protonation of the dianions (in terms of Hückel's approximation), the protophilic properties of which decrease in the same direction as in the radical-anions judging from the available qualitative data [106].

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The data presented in this review reveal certain characteristics of the metallation reactions involving the radical-anions and dianions of aromatic hydrocarbons. Metallation by radical-anions includes, together with their protonation, an electron transfer stage. The dianions react with proton donors as diacidic bases. However, in consequence of the high reduction potential of the dianions, there is a possibility of a side reaction involving electron transfer to the proton donor. The products of the protonation of the radical-anions and dianions (the carbanions of the dihydro-derivatives) are also highly reactive metallating agents. In the course of studies on metallation by radical-anions, an unusual feature was observed—an increase of their reactivity (protophilic properties) in the case of a strong interaction with the counterion. The details of the structure of the reactants, which determine the structure or the activated complex incorporating the cation, play an important role under these conditions.

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Karpov Physicochemical Institute
Moscow

U.D.C. 547.23:543.307

Methods for the Cleavage of N-N Bonds in Organic Compounds

M.F.Marshalkin and L.N.Yakhontov

In the review an attempt is made for the first time to give a systematic account of the available extensive literature data on the methods for the dissociation of N-N single bonds in organic compounds. Reductive and acid cleavage, various rearrangements, interaction with oxidants, and thermal and photochemical processes have been examined. In order to account for the characteristics of the dissociation of N-N bonds, data for the energy characteristics of the N-N and N≡N groups are adduced. The bibliography includes 274 references.

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I. INTRODUCTION

Processes involving the dissociation of N–N bonds in both cyclic and acyclic compounds occupy an important place in organic chemistry. They include the classical Fischer, Curtius, and Schmidt reactions, the benzidine rearrangement, and others, each of which has been the subject of serious and thorough reviews. However, there are no reviews giving a general account of different methods for the dissociation of N–N bonds. Even the familiar monograph of Weygand and Hilgetag[1], which constitutes a fairly complete encyclopedia of synthetic methods arranged systematically in accordance with the bond differences in the compounds, contains no section whatsoever dealing with the dissociation of N–N bonds. Other monographs[2-9], in which the general problems of the chemistry of organic compounds with N–N bonds are considered but the reactions involving the dissociation of such bonds are not specified, also fail to fill this gap.

A characteristic feature of a single bond between two nitrogen atoms is the low dissociation energy (37 kcal mole^{-1}) compared with other single bonds commonly encountered in organic compounds (for example the dissociation energy is 80 kcal mole^{-1} for C–C, 66 kcal mole^{-1} for C–N, and 64 kcal mole^{-1} for S–S).[10] On the other hand, the linkage with the highest bond multiplicity between nitrogen atoms (N≡N), which is characteristic of molecular nitrogen, has the maximum dissociation energy (225 kcal mole^{-1}) compared with the analogous C≡C (198 kcal mole^{-1}) and C≡N (209 kcal mole^{-1}) bonds[7]. In a saturated system, there is repulsion between the nitrogen *p* orbitals, which makes the N–N bond longer (1.40 Å)[11-13] than the sum of the radii of two nitrogen atoms (2 × 0.53 = 1.06 Å), while a characteristic feature of N≡N is the overlapping of the *p* orbitals, which causes additional bond stabilisation. In particular, the above characteristics are responsible for the behaviour of the relevant substances in chemical reactions. The dissociation of the saturated nitrogen–nitrogen bond takes place very rapidly, much more so than that of the C–C or C–N bonds, and, when competing reactions are possible, the dissociation of the N–N bond takes place preferentially and usually results in the formation of either the corresponding amino-derivative or of unstable products of the nitrene type with an electron sextet at the nitrogen atom. The latter can be stabilised in different ways via addition reactions, rearrangements, etc. The stability of molecular nitrogen noted above, the energy gain in its formation, and its capacity to be removed from the reaction sphere in the form of a gas also have a significant influence. In azides, azines, and other compounds, where the dissociation of N–N bonds with evolution of a nitrogen molecule is possible, this type of process usually takes place preferentially.

The above general features of the cleavage of N–N bonds can be readily traced in different types of reactions discussed in the present review. Naturally, within the framework of a journal article it is impossible to describe all cases of organic reactions involving the dissociation of N–N bonds. Therefore we thought it useful to describe in the review as fully as possible different types of processes at the expense of reducing the number of examples of each.

Together with a description of pioneer investigations, attention was concentrated on a selection of original papers reflecting most fully the scope of the method, the mechanism of the reactions, and their unusual course. The generally known classical reactions are not considered in the review. Whenever possible, references are given in all cases to review articles in which all the remaining literature is quoted.

II. REDUCTIVE CLEAVAGE OF N–N BONDS

The hydrogenolysis of N–N bonds is one of the most familiar methods of converting the various azines, azides, hydrazines, and their derivatives into the corresponding amines. The capacity of zinc in an acid medium to dissociate the N–N bond, observed by Curtius in the

reduction of benzylideneazine and its homologues to mono- and di-benzylamines[14], was subsequently used successfully for the synthesis of aromatic perfluorodiamines from hydrazones[15] in the course of the complete synthesis of sphingosine[16]. Various reducing agents are employed to convert arylhydrazones and hydrazines into amines in the synthesis of aminosugars[17-22] and aminoacids[23,24].

The reduction of arylhydrazones of α-ketoacids constitutes the basis of the synthesis of aminoacids via the mechanism

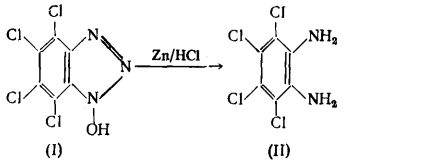
$$RCH(OAc)COOEt \rightarrow R{-}C(=N{-}NHPh)COOH \rightarrow R{-}CH(NH_2)COOH .$$

developed by Feofilaktov and coworkers[25-31].

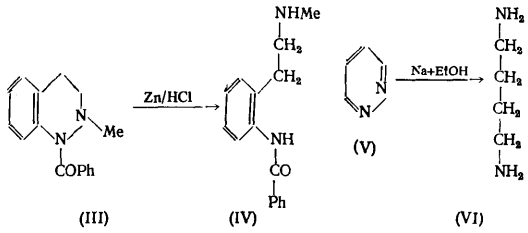
Catalytic methods have found extensive applications in the dissociation of N–N bonds in azines, hydrazines, hydrazides, and hydrazones[32-46]. Catalytic reduction has been used also for the conversion of sulphonyl hydrazides into sulphonamides[47].

Earlier studies on the reductive cleavage of N–N bonds in hydrazines and their derivatives by chemical and catalytic methods have been discussed[48-50] and other reports have dealt with the polarographic reduction of arylhydrazones[51,52].

The N–N bonds in heterocyclic N–N systems have also been successfully cleaved by reductive methods[34,38,53-55] and the conversion of, for example, the benzotriazole derivative (I) into *o*-phenylenediamine (II),[56] of tetrahydrocinnoline (III) into the *o*-aminoethylphenylamine derivative (IV),[57] of pyridazine (V) into 1,4-diaminobutane (VI,[58] etc. has been achieved.

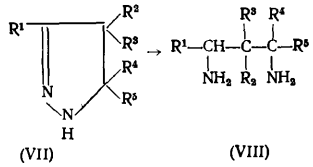


(I) (II)



(III) (IV) (VI)

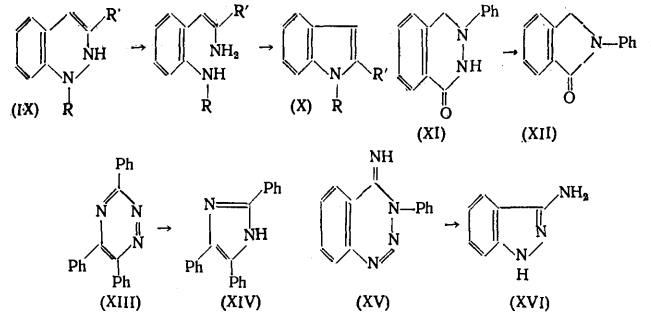
The hydrogenolysis of pyrazolines (VII) over a nickel catalyst constitutes the basis of the preparative synthesis of 1,3-diamines (VIII) developed by Kost and coworkers[59,60]:



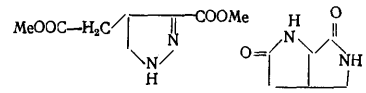
(VII) (VIII)

The hydrogenolysis of cyclic hydrazines derived from 3,5-dioxopyrazolidines over a nickel catalyst was investigated in detail by Moldaver and coworkers[61-63]. The electrochemical reduction of heterocyclic N–N compounds has been described in a review[64].

In many cases the diamines formed on reduction of cyclic hydrazine derivatives can recyclise, becoming converted during the reaction into other heterocycles. Indoles (X) from cinnolines (IX),[65-69] phthalimidine (XII) from dihydrophthalozolone (XI),[70] imidazole (XIV) from triazine (XIII),[71] and indazole (XVI) from benzotriazine (XVI)[72] have been obtained in this way:

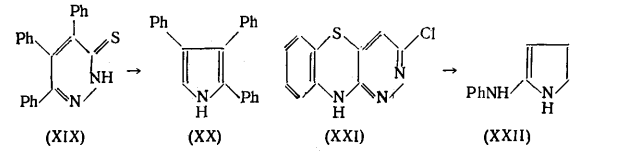


An interesting reaction was observed in the catalytic reduction of methyl 3-methoxycarbonylpyrazoline-4-acetate (XVII) where the diamine formed in the hydrogenation reaction is cyclised into a dilactam (XVIII):[73]



(XVII) (XVIII)

Unexpected results were obtained on heating 3-mercapto-4,5,6-triphenylpyridazine (XIX) with Raney nickel, when 2,3,4-triphenylpyrrole (XX) was isolated as the desulphurised product[74] and in the reduction of 5-chloro-3,4-diazaphenothiazine (XXI) in the presence of the same catalyst where the elimination of sulphur and the halogen was accompanied by the dissociation of the N–N bond, the elimination of ammonia, and the closure of the pyrroline ring with formation of compound (XXII):[75]



(XIX) (XX) (XXI) (XXII)

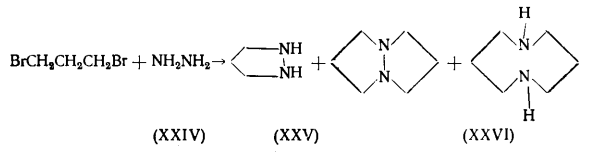
The cleavage of the N–N bond in 1-(2′-diethylaminoethyl)-2-phenylisopropylhydrazine (XXIII) on refluxing with hydrochloric acid without the addition of reducing agents was described by Elslager et al.[76]:

$$PhCH_2CH(Me)\underset{(XXIII)}{NHNH(CH_2)_2NEt_2} \longrightarrow$$
$$\rightarrow PhCH_2CH(Me)NH_2 + H_2N(CH_2)_2NEt_2 .$$

Probably a molecule of the initial compound (XXIII) behaves in this case as a reducing species; this mechanism is supported by the detection of phenylacetone in the reaction products.

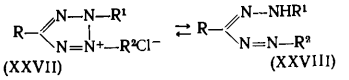
A mechanism involving a diarylnitrenium ion has been proposed for the cleavage of tetra-arylhydrazines under the influence of acids to diarylamines and a stable radical-cation[77] and the homolytic cleavage of N–N bonds in tetra-arylhydrazines has been discussed in two reports[79,80]. The oxidation–reduction reaction involving the initial compound evidently takes place when hydrazine interacts with 1,3-dibromopropane, which results in the formation,

together with pyrazolidine (XXIV) and a bicyclic hydrazine (XXV), also of bistrimethylenedi-imine (XXVI):[81]



(XXIV) (XXV) (XXVI)

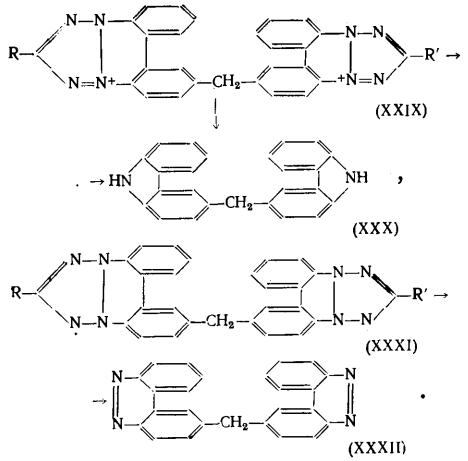
The reduction of quaternary tetrazolium salts (XXVII) with dissociation of the N–N bond and the formation of the formazan (XXVIII) takes place under the influence of bacteria, yeasts, germinating seeds[82], and also on treatment with ammonium sulphide[83] or on a cation-exchange resin treated with sodium dithionite[84]:



(XXVII) (XXVIII)

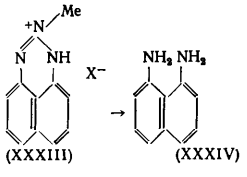
In the oxidation of formazan, quaternary tetrazolium salts are readily reformed[83]. The ease of the interconversion by a similar mechanism of substituted triazolium salts and 2-phenylamino-1-phenylazonaphthalenes made it possible to employ compounds of this kind as oxidation–reduction indicators of cobalt ions[85].

The conversion of quaternary bis-(2,3-*o*-diphenylenetetrazolium) salts (XXIX) into the corresponding carbazole (XXX) under the influence of zinc dust has been described; in the presence of sodium dithionite or hydrazine in an alkaline medium, free N-radicals (XXXI) are formed and reduced by nickel to phenazone (XXXII):[86]



(XXIX) (XXX) (XXXI) (XXXII)

The tendency of quaternary tetrazinium salts to undergo hydrogenolysis at N–N bonds has served as a basis for the preparation of 1,8-diaminonaphthalene (XXXIV) from 2-methyl-1*H*-naphtho[1,8-*de*]triazinium halides (XXXIII):[87]



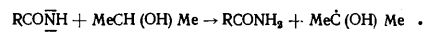
(XXXIII) (XXXIV)

The reduction of azides to the corresponding amines with cleavage of N–N bonds by both chemical and catalytic methods has been used to synthesise aminosugars[88–91] and aminosteroids[92]; methyl *p*-azidosulphonylcarbanilate is reduced by zinc in acetic acid to the corresponding sulphonamide[93].

When aryl azides are treated with hydrogen bromide, the N–N bonds are cleaved with simultaneous ring bromination; the following mechanism has been proposed to account for this process[94]:

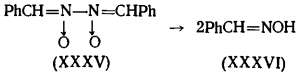


The reductive elimination of nitrogen with dissociation of the N–N bond in acid azides under the influence of isopropyl alcohol in the presence of the diethyl peroxydicarbonate has been regarded by Horner et al. as a radical reaction proceeding via the formation of radicals, and isopropyl alcohol followed by their interaction with azides via the following mechanism[95]:



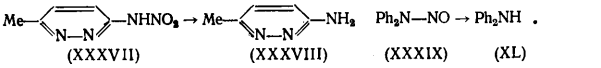
The reduction of acid azides by tributyltin hydride in the presence of azobisisobutyronitrile probably also proceeds via a radical mechanism[96].

There is an interesting case of the dissociation of the N–N bond in the reduction of benzaldehyde azine *NN'*-dioxide (XXXV) by ammonium sulphide in alcohol which gives a 78% yield of benzaldehyde oxime (XXXVI):[97]



(XXXV) (XXXVI)

Reductive cleavage of the N–N bond is also known for *N*-nitro- and *N*-nitroso-compounds: 6-methyl-3-nitraminopyridazine (XXXVII) is reduced in the presence of palladium to 3-amino-6-methylpyridazine (XXXVIII)[98] and *N*-nitrosodiphenylamine (XXXIX) is reduced by lithium aluminium hydride to diphenylamine (XL):[99,100]

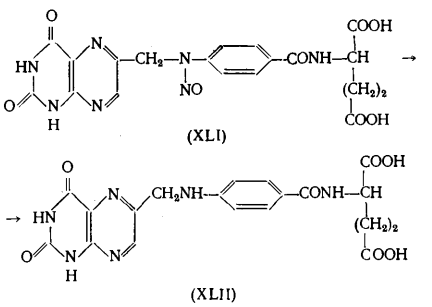


(XXXVII) (XXXVIII) (XXXIX) (XL)

III. ACID CLEAVAGE OF *N*-NITROSO- AND *N*-NITRO-DERIVATIVES

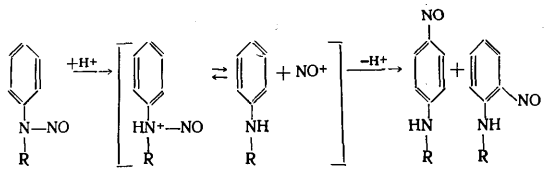
Together with the reductive cleavage of N–N bonds in *N*-nitro- and *N*-nitroso-compounds, the cleavage of compounds of this type by inorganic and organic acids, frequently in the presence of additives binding the nitro-groups and also binding or oxidising the nitroso-groups, has been described[101–105].

As an example, one may quote the denitrosation of *N*-[4-{[(2,4-dihydroxy-6-pteridyl)methyl]-*N*-nitrosoamino}benzoyl]glutamic acid (XLI) by hydrochloric acid in the presence of phenol in the course of the synthesis of the desaminohydroxy-analogue of folic acid (XLII)[105] and the cleavage of the N–N bond in *N*-nitro-compounds by hydrofluoric acid in the presence of anisole[106] or sulphuric acid with acetanilide[107]:

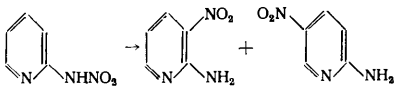


(XLI) (XLII)

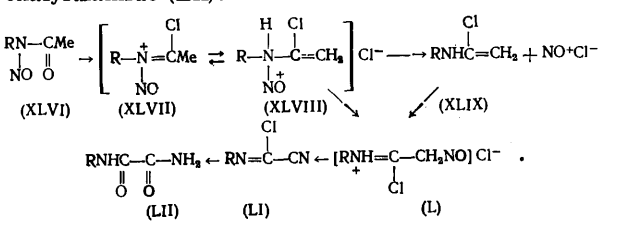
In certain cases the dissociation of the N–N bonds is accompanied by nitration or nitrosation of the denitrosated (or denitrated) compound itself and not of specially added substances with enhanced nucleophilic properties such as phenol, anisole, etc. Such rearrangements have been observed for the first time by Fischer and Hepp in the conversion of *N*-alkyl(aryl)-*N*-nitrosoanilines into the corresponding *p*-nitroso-derivatives [108]. Subsequently it was established that the nitroso-group can migrate not only to the *para*- but also to the *ortho*-position; it has been suggested that such rearrangement has a cationotropic mechanism [109–111]:



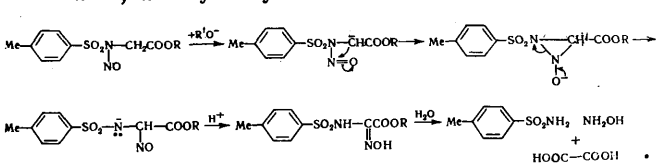
The isomerisation of 2-nitroaminopyridine (XLIII) into 2-amino-3-nitropyridine (XLIV) and 2-amino-5-nitropyridine (XLV): [112]



as well as rearrangements of the Fischer–Hepp type in many other aromatic nitramines [113–117] probably take place similarly. A different type of cleavage of the N–N bond was observed in the rearrangement of *N*-alkyl-*N*-nitrosamides (XLVI) to substituted oxalyldiamides under the influence of phosphorus pentachloride [118]. The mechanism of the rearrangement was associated with the formation of an intermediate iminochloride (XLVII) which isomerises to α-chlorovinylamine (XLVIII) with subsequent migration of the *N*-nitroso-group to the β-carbon atom of the vinyl residue either as a result of the elimination of nitrosyl chloride and its electrophilic addition to the double bond in compound (XLIX) or via an intramolecular shift with subsequent dehydration of compound (L) to the nitrile (LI). The final stage is the hydrolysis of (LI) to the *N*-substituted oxalyldiamide (LII):

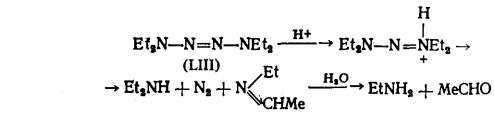


Under the influence of bases, the esters of *N*-nitroso-*N*-tosylglycine are cleaved into toluene-*p*-sulphonamide, oxalic acid, and hydroxylamine [119,120]:

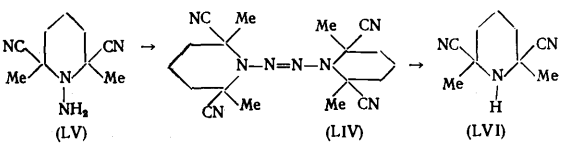


IV. THE CLEAVAGE OF AZINES

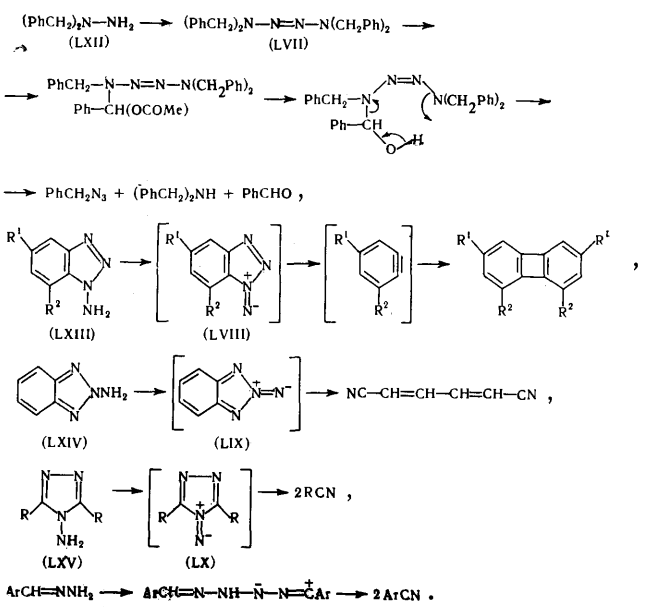
A common reaction involving the dissociation of N–N bonds is the cleavage of azines. For example, in acid tetraethyltetrazine (LIII) is converted into ethyl- and diethyl-amines, nitrogen, and acetaldehyde, the formation of which can be represented as follows [121]:



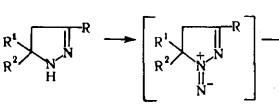
A similar acid cleavage of azines can be used in the synthesis of many carbohydrates [122] and some phenhomazine derivatives [103]. The oxidative deamination of *N*-aminopiperidine (LV) by potassium permanganate with subsequent treatment by hydrobromic acid probably also proceeds via the tetrazine (LIV); the final product of this reaction is 2,6-dicyano-2,6-dimethylpiperidine (LVI): [123]



Another reagent frequently used to deaminate heterocyclic *N*-amino-compounds is nitrous acid [123,124]. The oxidation of 1,1-disubstituted hydrazines of type (LVII), [125,126] 1-aminobenzotriazole (LXIII) and 2-aminobenzotriazole (LXIV), [127] 1-amino-1,3,4-triazoles (LXV), [128] and also arylhydrazones (LXVI) [129] by lead tetra-acetate proceeds via the corresponding tetrazines (LVII)–LXI):

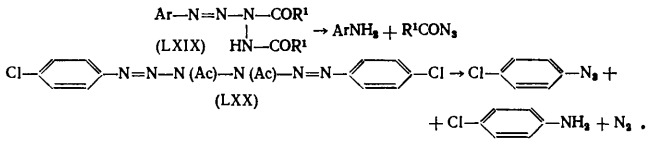


The triazine (LXVII) has been postulated as an intermediate in the nitrile cleavage of pyrazolines (LXVIII) under the influence of difluoroamine [130]:



Azines can be decomposed not only in acid [121–124] but also in alkaline media, as can be observed in the formation of acyl azides and aromatic amines [131] from the products of the reaction of 1,2-diacylhydrazines and arenediazonium

salts (LXIX) or in the alkaline cleavage of the hexaazadiene (LXX):[132]

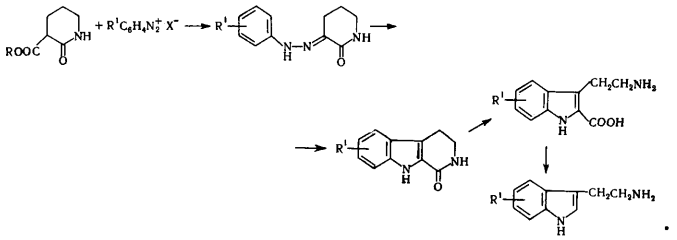


The thermal decomposition of azines with dissociation of N–N bonds has also been described[133–135].

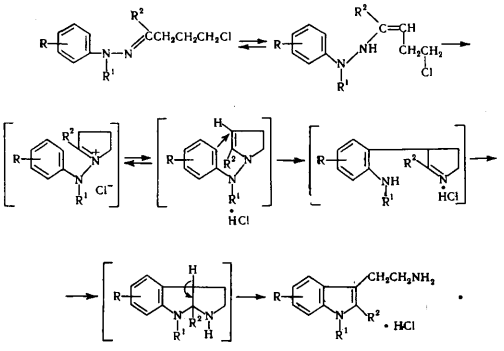
V. REACTIONS OF ARYLHYDRAZONES ANALOGOUS TO THE FISCHER REACTION

The very familiar Fischer reaction involving the synthesis of indole derivatives with dissociation of N–N bonds has been discussed in fine detail in many recent reviews[136–139], which obviates the necessity to analyse in the present report the extensive literature on this question. At the same time, one should mention that the great interest in the Fischer reaction and the detailed study of this method in various systems have led to the development of many other reactions analogous to the Fischer cyclisation and also involving the dissociation of N–N bonds.

Here mention must be made in the first place of the reaction of Abramovitch and Shapiro which has found extensive application in the synthesis of tryptamines and which consists in the interaction of diazonium salts and 3-alkoxycarbonylpiperidine-2-ones with subsequent cyclisation, opening of the piperidinone ring, and decarboxylation[140]:

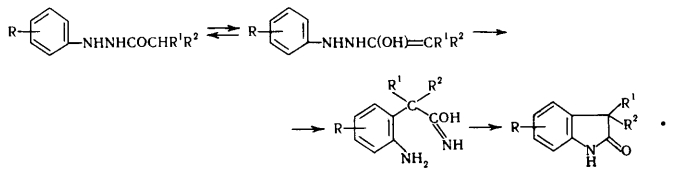


A novel method of synthesising tryptamines and homotryptamines in one step from arylhydrazones of γ- and δ-halogenocarbonyl compounds has been described by Grandberg and coworkers[141–145]:

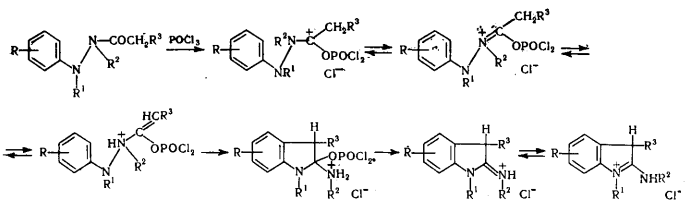


Cyclic enamines have been introduced into the reaction with hydrazines instead of halogenocarbonyl compounds[146]; the use of α-substituted γ-halogenoketones leads to eseroline derivatives[147,148].

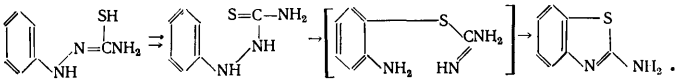
The synthesis of oxindoles from carboxylic acid arylhydrazides has been developed by Bruner[149–153]:



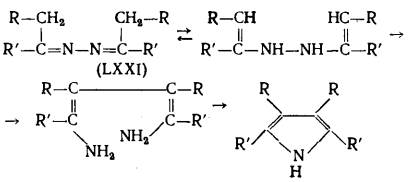
Kost and coworkers suggested a method for the synthesis of 2-aminoindoles based on the interaction with phosphoryl chloride of the arylhydrazides of carboxylic acids containing a methylene group in the α-position in the acid residue[154]:



Even earlier, Fischer and Besthorn[155] and then other workers[156] showed that phenylthiosemicarbazide formed from phenylhydrazine and thiocyanate readily cyclises to 2-aminobenzothiazole when acted upon by acids:

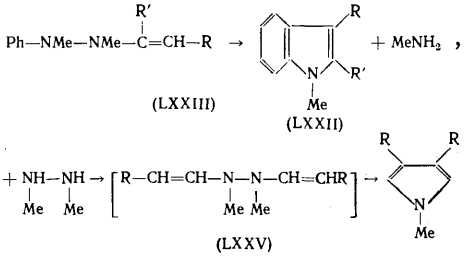


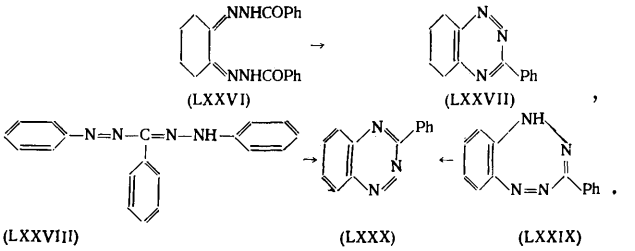
The synthesis of pyrrole derivatives by treating tetrasubstituted azines (LXXI) with acid catalysts has been developed by Piloty[157]:



A similar reaction has been used also to prepare octahydrocarbazole from cyclohexanone azine[158,159].

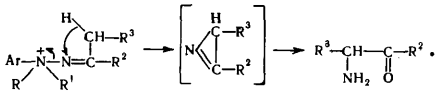
Other processes involving the dissociation of N–N bonds in *N*-substituted hydrazines, hydrazones, and their cyclic analogues are also closely related to the Fischer cyclisation: the synthesis of indoles (LXXII) from *NN'*-dimethylene-*N*-phenylhydrazines (LXXIII),[160] of symmetrical *N*-methylpyrroles (LXXIV) from 1,2-dimethylhydrazines (LXXV),[161] the rearrangement of the bisbenzoylhydrazone of cyclohexane-1,2-dione (LXXVI) to 3-phenyl-5,6-cyclohexeno-1,2,4-triazine (LXXVII),[162] and the rearrangement of 1,3,5-triphenylformazan (LXXVIII) and *C*-phenyl-*NN'*-*o*-phenyleneformazan (LXXIX) to 3-phenyl-5,6-benzo-1,2,4-triazine (LXXX):[163,164]





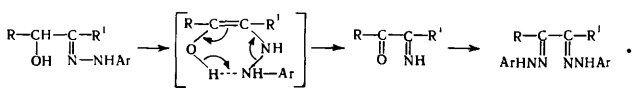
(LXXVI) (LXXVII) (LXXVIII) (LXXX) (LXXIX)

The dissociation of the N—N bond with the Neber rearrangement has been described for quaternary derivatives of arylhydrazones of ketones with an α-hydrogen atom [compounds (LXXXI)] [165-167] which, in contrast to the analogous aldehyde derivatives, are incapable of the nitrile rearrangement. It has been shown that the process is stereospecific, probably proceeds via a three-membered cyclic transition state (LXXXII), [168-170] and leads to the formation of α-aminoketones (LXXXIII):



(LXXXI) (LXXXII) (LXXXIII)

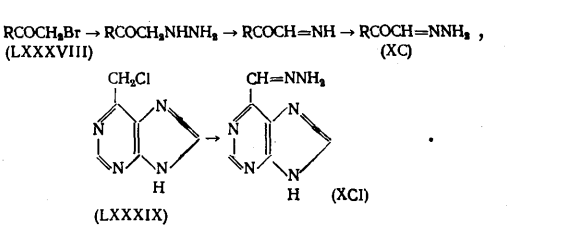
Many studies have been made on the dissociation of the N—N bond in the arylhydrazone of α-hydroxycarbonyl compounds (LXXXIV) with their conversion into osazones (LXXXV). [171-175] The mechanism of this reaction, which is important in sugar chemistry, has been investigated by Shemyakin and coworkers using labelled nitrogen [174]. It was shown that the arylamine is split off initially via a six-membered transition state, for which the authors postulate the structure (LXXXVI), and the monoimine of the α-diketone (LXXXVII) is formed and then converted into compound (LXXXV) under the influence of the arylhydrazine:



(LXXXIV) (LXXXVI) (LXXXVII) (LXXXV)

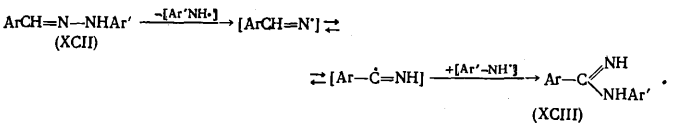
The monoimines of α-diketones (LXXXVII) can be isolated in the form of *N*-acetyl derivatives when compounds (LXXXIV) are cleaved in acetic acid; the addition of *o*-phenylenediamine leads to the formation of substituted quinoxalines [176,177].

Reactions of hydrazine with phenylacyl halides (LXXXVIII) [178] and 6-chloromethylpurine (LXXXIX) [179] apparently also proceed via intermediate amino-derivatives and lead to the formation of the corresponding hydrazones (XC) and (XCI):



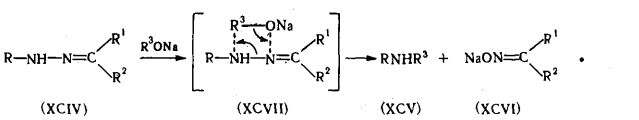
(LXXXVIII) (XC) (LXXXIX) (XCI)

Together with the well known benzidine rearrangement [180-186], it is appropriate to mention in this section the amidine rearrangement discovered by Robev [187-190], which is observed when the arylhydrazones of aldehydes (XCII) are heated with strong bases; it is initiated by atmospheric oxygen, probably has a radical mechanism [191,192], and leads to the formation of *N*-substituted amidines (XCIII):



(XCII) (XCIII)

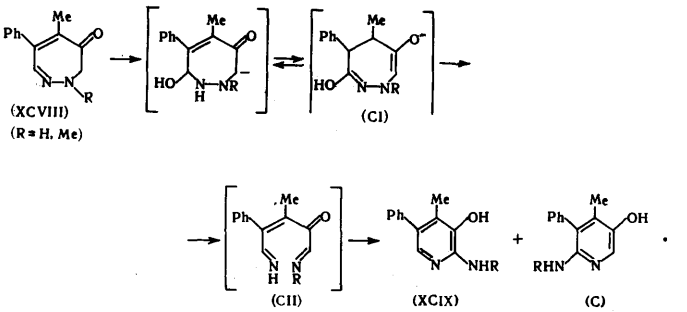
A new type of cleavage of the N—N bond in pyridyl-(aryl)hydrazones (XCIV) under the influence of alkali metal alkoxides has been described by Yakhontov and Marshalkin [193-195]. The reaction products are *N*-monoalkylpyridyl-(or aryl)amines (XCV) and the sodium derivatives of the *syn*-oximes of the carbonyl component (XCVI). The reaction takes place particularly smoothly with (4-pyridyl)- and (3-pyridyl)-hydrazones of aromatic aldehydes. Under these conditions, the corresponding pyridylhydrazines are cleaved only to the aminopyridines and *N*-alkylation products are not formed. It has been suggested that the reaction of alkoxides with compounds (XCIV) proceeds via a four-membered cyclic transition state (XCVII) with simultaneous dissociation of the N—N bond in the hydrazone and the C—O bond in the attacking alkoxide:



(XCIV) (XCVII) (XCV) (XCVI)

VI. REARRANGEMENT OF HETEROCYCLIC 1,2-DIAZA-SYSTEMS

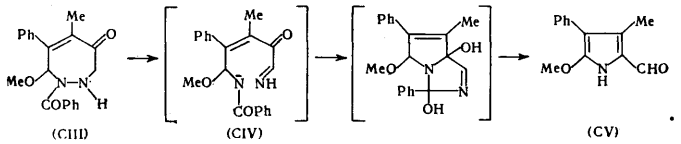
The rearrangements of heterocyclic 1,2-diaza-systems investigated in recent years are related to the methods of synthesising α-imino- and α-hydrazino-ketones described in the preceding section. An example of this type of rearrangement is the conversion of 2,3-dihydro-5-methyl-6-phenyl-1,2-diazepin-4-one (XCVIII) under the influence of alkali to substituted α-aminopyridines (XCIX) and (C), which probably takes place as a result of the nucleophilic attack on compound (XCVIII) by the hydroxide ion in the 3- and 7-positions with formation of the enolate (CI); the β-elimination processes involving the last product lead to the di-imineketone (CII), which can cyclise in two ways with conversion into the isomers (XCIX) and (C): [176,196]



(XCVIII) (R = H, Me) (CI) (CII) (XCIX) (C)

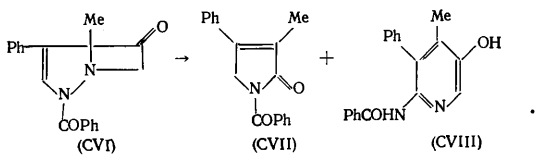
β-Elimination does not occur in the case of 1-benzoyl-7-methoxy-5-methyl-6-phenyltetrahydrodiazepin-4-one (CIII), since the anion (CIV) formed after the dissociation of the N—N bond is stabilised by the amide carbonyl and

a retro-Michael condensation takes place with formation of the pyrrole (CV):[197]



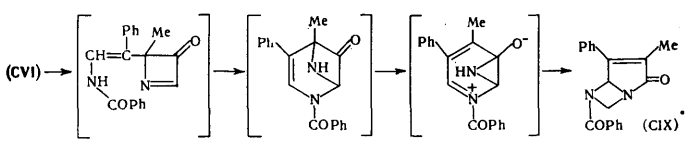
(CIII) (CIV) (CV)

It is suggested that the rearrangement of the substituted 2-benzoyl-1,2-diazabicyclo[3,2,0]hept-3-en-6-one (CVI) on refluxing in methanol to derivatives of pyrrole (CVII) and α-aminopyridine (CVIII) also proceeds via a derivative of 2,3-dihydro-1,2-diazepin-4-one[198,199]:



(CVI) (CVII) (CVIII)

Compound (CVI) undergoes a more complex rearrangement in boiling benzene, where 6-benzoyl-3-methyl-4-phenyl-1,6-diazabicyclo[3,2,0]hept-3-en-3-one (CIX) is formed by a mechanism analogous to the cleavage of α-hydrazinocarbonyl compounds[198]:

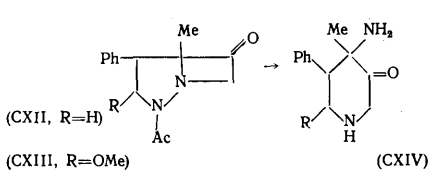


(CIX)

In an alkaline medium compound (CVI) is cleaved with formation of an acyclic enaminoketone (CX) and a saturated benzoylaminoketone (CXI):[198,199]

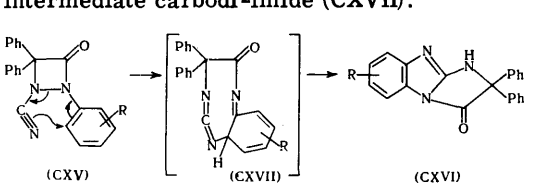
$$\text{CVI} \rightarrow \underset{\text{(CX)}}{H_2NCH{=}C(Ph)Ac} + \underset{\text{(CXI)}}{PhCONHCH_2CH(Ph)Ac}\ .$$

When bases act on 2-acetyl-5-methyl-4-phenyl-1,2-diazabicyclo[3,2,0]heptan-6-one (CXII) and its 3-methoxy-derivative (CXIII), a rearrangement takes place with dissociation of the N—N bond and the formation of substituted 4-aminopiperidin-3-ones (CXIV):[176,198]



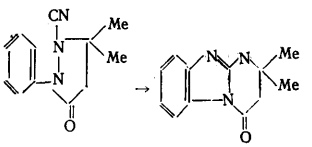
(CXII, R=H) (CXIII, R=OMe) (CXIV)

An interesting thermal rearrangement takes place in 1-aryl-2-cyano-3,3-diphenyldiazetidin-4-ones (CXV), which are converted in high yields into imidazo[1,2-*a*]-benzimidazole derivatives (CXVI), probably via the cleavage of the N—N bond and subsequent transannular cyclisation of the intermediate carbodi-imide (CXVII):[200]

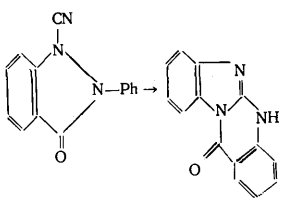


(CXV) (CXVII) (CXVI)

Probably 2-cyano-3,3-dimethyl-1-phenylpyrazolidin-5-one (CXVIII) is converted via a similar mechanism into 1,2,3,4-tetrahydro-2,2-dimethyl-4-oxopyrimido[1,2-*a*]-benzimidazole (CXXI)[201] and 1-cyano-2-phenyl-3-indazolone (CXX) is likewise converted into benzimidazo-[2,1-*b*]-12-quinazolone (CXXI):[201]

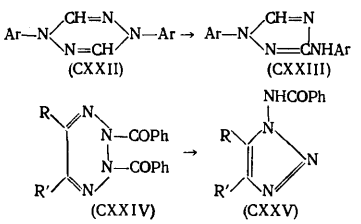


(CXVIII) (CXIX)



(CXX) (CXXI)

Tetrazine-triazole rearrangements, which also involve the dissociation of N—N bonds, constitute another type of rearrangement of heterocyclic 1,2-diaza-systems. They include the conversion of 1,4-diaryl-1,4-dihydro-1,2,4,5-tetrazines (CXXII) by sodium ethoxide into 3-arylamino-1,2,4-triazoles (CXXIII)[202] and of *C*-substituted 2,3-dibenzoyl-2,3-dihydro-1,2,3,4-tetrazines (CXXIV) in acid or neutral media into benzamido-1,2,3-triazoles (CXXV):[203-205]



(CXXII) (CXXIII) (CXXIV) (CXXV)

The conversion of 1-arylalkylindazoles on treatment with sodamide into 2-aryl-4-quinazolones discovered by Simonov et al.[206] can also be formally regarded as a rearrangement of heterocyclic 1,2-diazasystems.[206] However, this reaction has the mechanism of the nitrile rearrangement and can be more usefully considered in the next section of the review.

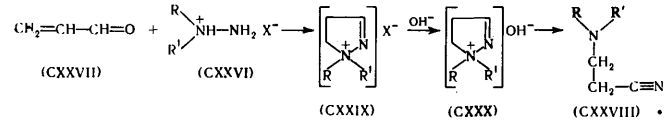
VII. THE NITRILE REARRANGEMENTS

In 1910 Arbuzov observed that, on heating with Lewis acids, the phenylhydrazones of aliphatic aldehydes undergo a rearrangement with dissociation of the N—N bond, the elimination of aniline, and the formation of a nitrile[207]:

$$R{-}CH{=}N{-}NHPh \rightarrow R{-}C{\equiv}N + PhNH_2\ .$$

Subsequently Kost, Grandberg and coworkers showed that this reaction is common to compounds of the type $RCH{=}N{-}N(R^1)R^2$ and suggested that it proceeds via the formation of a complex of the hydrazone with the Lewis acid, a far shift of the electron pair of the N—N bond, the formation of a δ^+ charge on the neighbouring carbon atom, and subsequent deprotonation with dissociation of the N—N bond[208-211]. A similar rearrangement takes place also when the hydrochlorides of pyrazoline derivatives are heated[212,213].

Ioffe and Zelenin observed that the condensation of asymmetric dialkylhydrazines (CXXVI) with acrolein (CXXVII) involves a rearrangement with formation of β-dialkylaminopropionitriles (CXXVIII) for which it has been established that the process proceeds via the quaternary pyrazolinium derivatives (CXXIX) and (CXXX) according to the mechanism [214-216]:

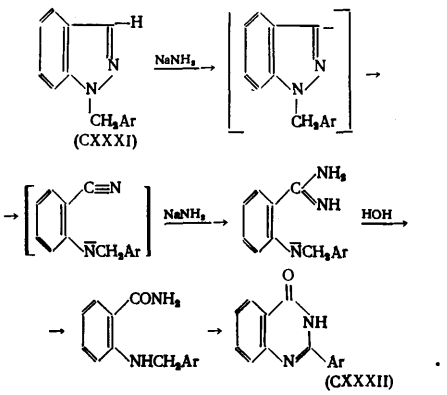


(CXXVII) (CXXVI) (CXXIX) (CXXX) (CXXVIII)

A similar nitrile cleavage of quaternary hydrazinium derivatives was observed in other instances also [217-221] and Grandberg and Naumov showed that the N–N bonds in compounds of this type are more labile than the C–N bond in quaternary ammonium bases [217].

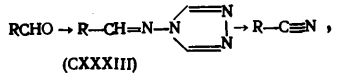
The nitrile rearrangement of hydrazones can be achieved not only under the influence of Lewis acid but also in reactions in the presence of various nucleophilic agents (sodamide, alkalies, etc.) [208,209,222-226] and apparently proceeds via a β-elimination mechanism: the nucleophilic agent attacks the hydrogen atom at the C=N double bond and the highly polarised N–N bond in the anion formed after deprotonation is readily dissociated under the influence of heat [209].

In many reactions this process does not stop at the nitrile stage, the nitrile being converted further into an amidine and an amide capable of cyclising into 4-quinazolone derivatives, as happens in the conversion, mentioned above, of 1-arylalkylindazoles (CXXXI) in the presence of sodamide into 2-aryl-4-quinazolones (CXXXII): [206,225]



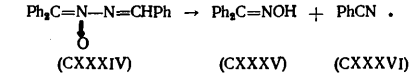
(CXXXI) (CXXXII)

The nitrile rearrangement is probably the final stage of the cleavage reactions of the azines (LXIV), (LXV), (LXVI), (LXVII), etc., described above (Section IV) and constitutes the basis of the method for the conversion of aldehydes into nitriles via 1-amino-1,2,4-triazoles derivatives (CXXXIII) proposed by Becker and Timpe [227]:



(CXXXIII)

as well as the conversion of aldehydes into nitriles via hydrazonium salts [220,228,229]. The polarisation of N–N bonds in the conversion from azines and hydrazones into their *N*-monoxides also promotes the cleavage of these compounds via a mechanism of the nitrile rearrangement type [230,231], as happens, for example, in the thermal decomposition of the azine *N*-monoxide (CXXXIV) to the corresponding oxime (CXXXV) and nitrile (CXXXVI): [230]

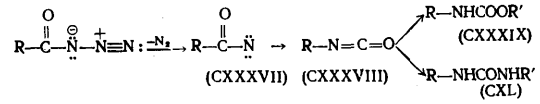


(CXXXIV) (CXXXV) (CXXXVI)

The thermal cleavage of non-oxidised azines and hydrazones, in which the polarisation of the N–N bond is less marked, proceeds with greater difficulty and the products of the nitrile rearrangement are obtained in lower yields [233-234]. It has been suggested that in such cases the reactions have a radical mechanism.

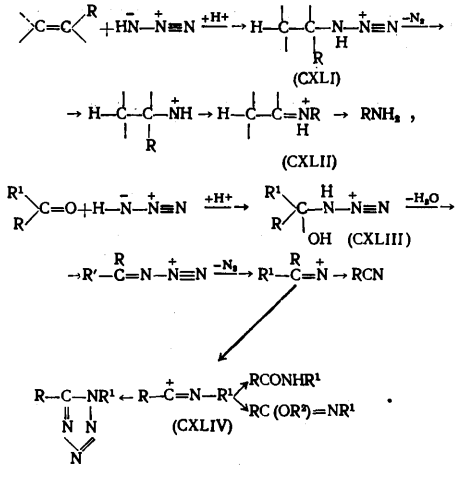
VIII. SEXTET REARRANGEMENTS OF THE TYPE OF THE CURTIUS AND SCHMIDT REACTIONS

The conversion of acid azides into isocyanates with cleavage of the N–N bond and the evolution of a nitrogen molecule, called the Curtius reaction, proceeds via the intermediate formation of a product (CXXXVII) with an electron sextet, the rearrangement of which takes place owing to the tendency of nitrogen to acquire the missing electrons from the adjacent carbon atom. As a result of the migration of the alkyl or aryl residue from compound (CXXXVII), the isocyanate (CXXXVIII) is formed and can be isolated from non-polar solvents; in the presence of alcohols it is converted into carbamic acid esters (CXXXIX) and on treatment with ammonia or amines it gives rise to substituted ureas (CXL):



(CXXXVII) (CXXXVIII) (CXXXIX) (CXL)

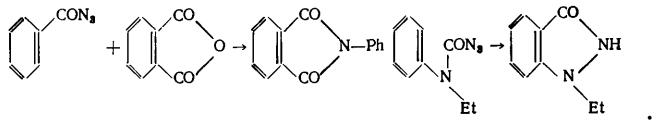
The Schmidt reaction, which consists in the interaction of equivalent amounts of hydrazoic acid and a carbonyl compound or an olefin in the presence of strong inorganic acids, has a similar mechanism. After the scission of nitrogen and the rearrangement, protonated *N*-substituted ketimines (CXLI) are formed from the adducts with olefins (CXLII) and can be readily hydrolysed to the corresponding amines. In the adducts with aldehydes (CXLIII, R′ = H), the sextet is usually stabilised via deprotonation with formation of a nitrile and the interaction of HN_3 with ketones entails a rearrangement with migration of the alkyl or aryl group, the resulting carbonium ion (CXLIV) being converted into amides on reaction with water, into iminoethers on reaction with alcohols, and into tetrazoles on reaction with an excess of HN_3:



(CXLI) (CXLII) (CXLIII) (CXLIV)

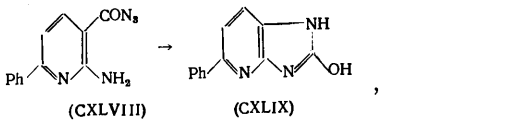
The Curtius and Schmidt reactions constitute important preparative methods for the synthesis of different classes of compounds: amines, amides, urethanes, substituted ureas, etc., which have been thoroughly investigated in a large number of instances and have been discussed in detail in many reviews [235-237]. This makes it unnecessary to consider them in detail here. Probably attention should be concentrated on sextet rearrangements of the type of the Curtius and Schmidt reactions, not included in the above reviews, which takes place with dissociation of N–N bonds and lead to the formation of more complex products.

As examples of reactions of this type, one may quote the formation of *N*-phenylphthalimide (CXLV) on heating benzoyl azide with phthalic anhydride [238] or the rearrangement of *N*-ethyl-*N*-phenylcarbamoyl azide (CXLVI) in boiling xylene to 1-ethyl-3-indazolone (CXLVII): [239]

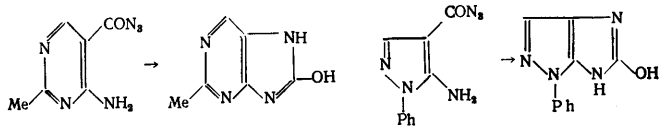


(CXLV) (CXLVI) (CXLVII)

When 2-amino-6-phenylnicotinoyl azide (CXLVIII) is heated in xylene, a quantitative yield of 2-hydroxy-6-phenylimidazo[4,5-*b*]pyridine (CXLIX) is obtained [240]. The thermal cleavage of the azides of 4-amino-2-methylpyrimidine-5-carboxylic (CL) and 5-amino-1-phenylpyrazole-4-carboxylic (CLI) acids takes place similarly [241]:

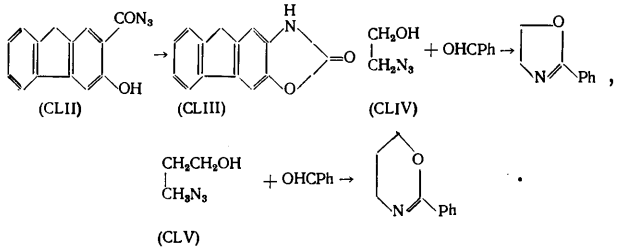


(CXLVIII) (CXLIX)



(CL) (CLI)

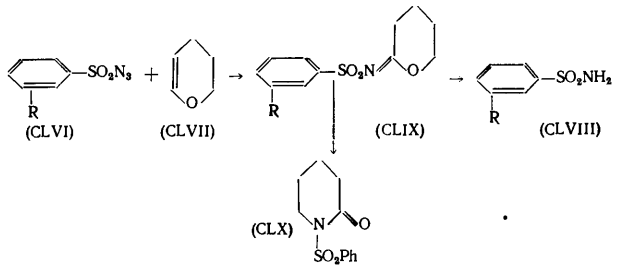
The rearrangement of the azides of 3-hydroxyfluorene-2-carboxylic acid (CLII) also leads to the closure of a new ring: the formation of 5*H*-fluoreno[2,3-*d*]oxazolidin-2-one (CLIII). [242] The closure of the oxazolidine or dihydrooxazine ring takes place also on heating of β- and γ-hydroxyalkyl azides, (CLIV) and (CLV), with benzaldehyde in the presence of sulphuric acid [243]. Probably this process proceeds via the mechanism of the Schmidt reaction with dehydration at the imino-derivative stage. Aliphatic and alicyclic carbonyl compounds do not enter into this reaction, in contrast to aromatic aldehydes:



(CLII) (CLIII) (CLIV)

(CLV)

Sulphonylazides usually do not undergo the Curtius rearrangement. However, high yield of *m*-nitrobenzenesulphonamide (CLVIII, R = NO_2) was obtained on heating in alcohol *m*-nitrobenzenesulphonylazide (CLVI, R = NO_2) and dihydropyran (CLVII). [244] Evidently the sextet formed after the dissociation of the N–N bond and evolution of nitrogen is in this case stabilised by the addition of a molecule of (CLVII) and the formation of 2-(*m*-nitrobenzenesulphonylimino)tetrahydropyran (CLIX, R = NO_2), which is cleaved in alcohol to compound (CLVIII, R = NO_2). [245] Similar reactions with dissociation of the N–N bond have been observed also for unsubstituted benzenesulphonyl azide (CLVI, R = H), where the hydrolysis of compound (CLIX, R = H) results in the formation of benzenesulphonamide (CLVIII, R = H) and the thermal rearrangement of (CLIX, R = H) yields *N*-phenylsulphonylpiperidin-2-one (CLX): [245]



(CLVI) (CLVII) (CLIX) (CLVIII)

(CLX)

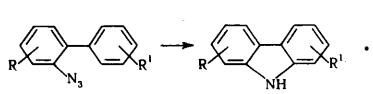
One should probably also include among sextet rearrangements the conversion of hydrazones into amides under the influence of sodium nitrite and concentrated sulphuric acid [246,247]:

$$R_2C{=}NNH_2 \rightarrow RCONHR + N_2 ,$$

and also the rearrangement of 1-acetylimino-1-methyl-2-phenylpyrrolidine (CLXI), discovered by Wawzonek, which results in the formation of methyl isocyanate (CLXII) and 1-methyl-2-phenylpyrrolidine (CLXIII). [248]

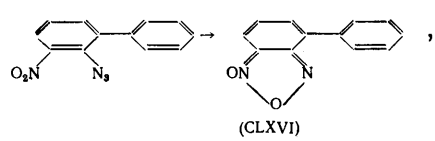
IX. THERMAL CYCLISATION OF AZIDES

The thermal cyclisation of azides discovered by Smith and Brown, which takes place with dissociation of the N–N bond [249], constitutes an important method for the synthesis of heterocyclic systems and merits special discussion. Initially this reaction was developed for the synthesis of carbazoles (CLXIV) from 2-azidobiphenyls (CLXV) and it was found that with 5-nitro- or 4′-5-dinitro-derivatives (CLXV) the yields of the tricyclic derivatives were appreciably higher than in the cyclisation of the 5-bromo- and 3,5-dibromo-derivatives or the unsubstituted compound (CLXV): [249]

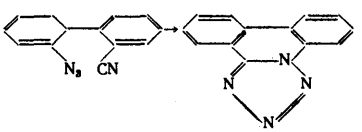


(CLXV) (CLXIV)

The 3-nitro-derivative of compound (CLXV) is converted into 4-phenylbenzofuroxan (CLXVI), i.e. the cyclisation involves the nitro-group, while with 2-azido-2′-cyanobiphenyl the process takes place without the evolution of nitrogen with formation of tetrazolophenanthridine (CLXVII): [250]

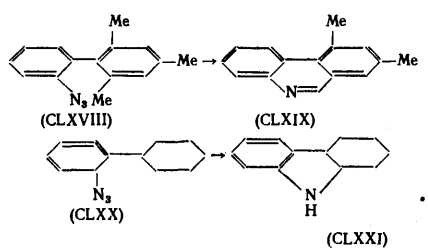


(CLXVI)



(CLXVII)

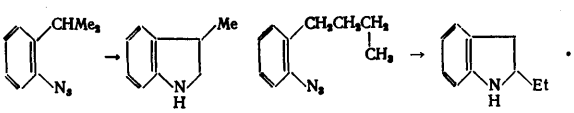
Subsequently the thermal cyclisation of azides were extended to aza- and thia-analogues of compound (CLXV) [251] and it was also shown that an analogous reaction with dissociation of the N–N bond can occur with participation of aliphatic residues. Thus the cyclisation of 2-azido-2′,4′,6′-trimethylbiphenyl (CLXVIII) yielded phenanthridine (CLXIX) [252] and hexahydrocarbazole (CLXXI) was obtained from *o*-azidophenylcyclohexane (CLXX): [252]



(CLXVIII) (CLXIX)

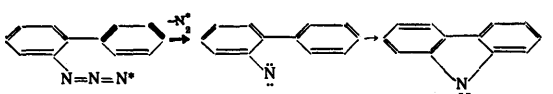
(CLXX) (CLXXI)

The application of the same reaction to *o*-azidoisopropylbenzene (CLXXII) and *o*-azidobutylbenzene (CLXXIII) permitted a new synthesis of indolines (CLXXIV) and (CLXXV), [252,253] in which tetrahydroquinolines and products of the reductive cleavage of the N–N bonds in the azides (CLXXII) and (CLXXIII) (*o*-alkylanilines) were obtained as side products:



(CLXXII) (CLXXIV) (CLXXIII) (CLXXV)

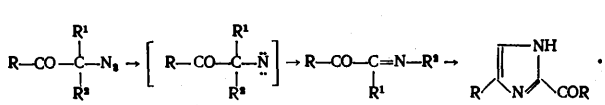
It was established with the aid of labelled nitrogen that the cyclisation of azides proceeds via a nitrene (CLXXVI) stage [250,254] with evolution of molecular nitrogen containing the label:



(CLXXVI)

This mechanism is supported also by the formation of phenyl isocyanate on thermal decomposition of phenyl azide in carbon monoxide and of carbazole and 2-biphenylyl isocyanate from 2-azidobiphenyl [255]. A similar mechanism for the decomposition of azides was proposed for the process catalysed by iridium salts [258].

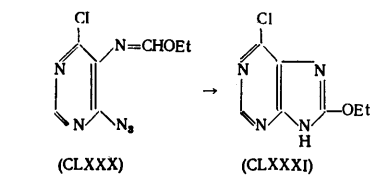
A radical process with formation of intermediate nitrenes has also been postulated for the thermal cleavage of α-azidocarbonyl compounds (CLXXVII), where the substituent R^2 was found to migrate after the elimination of the nitrogen molecule (the ease of migration increases in the sequence $CH_3 < C_6H_5 < H$) and a monoimino-derivative (CLXXVIII) of the α-dicarbonyl compound was formed:



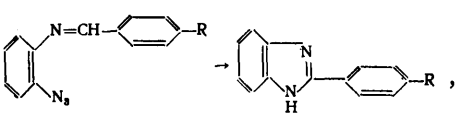
CLXXVII) (CLXXVIII) (CLXXIX)

This reaction has been used for the synthesis of substituted imidazoles (CLXXIX) from α-azidocarbonyl compounds (CLXXVII, $R^1 = R^2 = H$) via (CLXXVIII, $R^1 = R^2 = H$) by dimerisation of the latter with elimination of water [257].

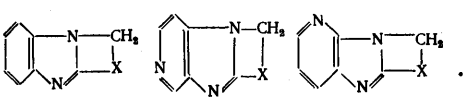
Another method for the synthesis of the imidazole ring via the thermal cyclisation of azides has been described in connection with a new synthesis of purines, whereby 6-chloro-8-ethoxypurine (CLXXXI) was obtained on heating 4-azido-6-chloro-5-ethoxymethyleneiminopyrimidine (CLXXX). [258] 2-Arylbenzimidazoles (CLXXXIII) were obtained similarly in almost quantitative yields from 2-azidobenzylideneanilines (CLXXXII) [259] and tricyclic derivatives of benzimidazole (CLXXXIV) and pyridoimidazole, (CLXXXV) and (CLXXXVI), were obtained from *N*-(*o*-azidophenyl)- or *N*-(3-azido-4-pyridyl)-derivatives of pyrrolidines, piperidines, and morpholines [260]:



(CLXXX) (CLXXXI)



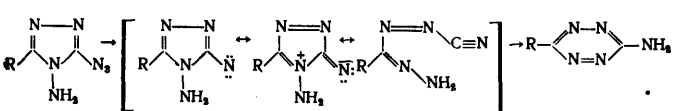
(CLXXXII) (CLXXXIII)



(CLXXXIV) (CLXXXV) (CLXXXVI)

(X=(CH$_2$)$_2$; (CH$_2$)$_3$; —CH$_2$OCH$_2$—)

On heating with chlorobenzene, the corresponding 4-amino-3-azido-s-triazoles (CLXXXVII) are converted in almost quantitative yields into 3-amino-1,2,4,5-tetrazines (CLXXXVIII), [261] which constituted a convenient method for the synthesis of symmetrical tetrazines. The process probably proceeds via a stage in which a nitrene is formed and exists in one of the canonical forms—the acylic nitrile (CLXXXIX) – which cyclises to (CLXXXVIII):



(CLXXXVII) (CLXXXIX) (CLXXXVIII)

Various reactions of nitrenes are considered in greater detail in special reviews [254,262–265].

X. PHOTOCHEMICAL DISSOCIATION OF N–N BONDS

In the last decade publications on the photochemical dissociation of N–N bonds in organic compounds have appeared with increasing frequency. One of the first reports in this field concerned the photochemical cleavage of acetaldehyde azine and benzaldehyde azine to the corresponding nitriles [266,267]. The photolysis was achieved in the presence of benzophenone and proceeded via the mechanism

$$Ph_2C{=}O \xrightarrow{h\nu} Ph_2\dot{C}{-}O^{\bullet},$$

$$Ph_2\dot{C}{-}O^{\bullet} + PhCH{=}N \cdot N{=}CHPh \rightleftarrows Ph\dot{C}{=}N \cdot N{=}CHPh + Ph_2\dot{C}{-}OH,$$

$$Ph\dot{C}{=}N \cdot N{=}CHPh + Ph_2C{=}O \rightarrow 2PhCN + Ph_2\dot{C}{-}OH.$$

The photochemical decomposition of aliphatic and aromatic *N*-nitrosoamines (CXC) leads to the corresponding amines (CXCI) and amidoximes (CXCII):[268]

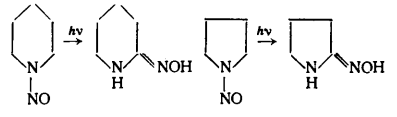
$$\underset{\text{(CXC)}}{PhCH_2N(NO)CH_2Ph} \xrightarrow[-NO^{\cdot}]{h\nu} \underset{\text{(CXCIII)}}{PhCH_2\dot{N}CH_2Ph},$$

$$\text{(CXCIII)} + \text{(CXC)} \rightarrow PhCH_2NHCH_2Ph + \underset{\text{(CXCI)}}{PhCH_2N(NO)\dot{C}HPh},$$

$$PhCH_2N(NO)\dot{C}HPh \rightarrow PhCH_2N{=}CHPh + NO^{\cdot},$$

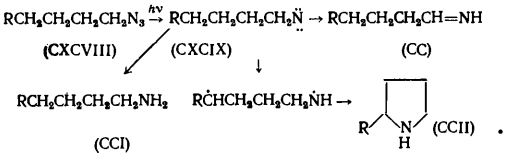
$$\text{(CXCIII)} \xrightarrow{+\dot{N}OH} PhCH_2NH{-}CH(\overset{+}{N}OH)Ph \xrightarrow{-H^+} \underset{\text{(CXCII)}}{PhCH_2NHC(=NOH)Ph}.$$

When *N*-nitrosopiperidine (CXCIV) or *N*-nitrosopyrrolidine (CXCV) is irradiated with ultraviolet light in aqueous methanol containing hydrochloric acid, the amidoximes (CXCVI) and (CXCVII) are formed in high yields[269]:



(CXCIV) (CXCVI) (CXCV) (CXCVII)

The photolysis of the non-aromatic azides (CXCVIII) results in the formation of the nitrenes (CXCIX) which can then react in three different ways: (a) they can isomerise to the imines (CC); (b) they can split off hydrogen from solvent molecules and be converted into amines (CCI); (c) they can undergo 1,5-deprotonation with cyclisation to pyrrolidines (CCII):[264,270]

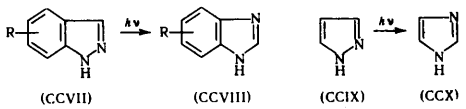


On direct irradiation in isopropyl alcohol, particularly in the presence of added benzophenone, sulphonyl azides (CCIII) are converted via a radical chain mechanism into the sulphonamides (CCIV). The process is catalysed by iron(III) chloride and is accelerated by heat[271].

On irradiation in cyclohexane, the azides of aliphatic carboxylic acids (CCV) are converted into the amides (CCVI). The reaction is sensitised by acetophenone[272]:

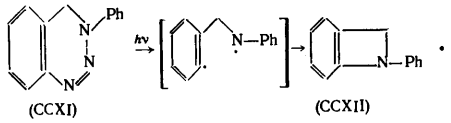
$$\underset{\text{(CCV)}}{C_nH_{2n+1}CON_3} \xrightarrow{h\nu} \underset{\text{(CCVI)}}{C_nH_{2n+1}CONH_2}.$$

Unexpected reactions are observed when certain heterocyclic 1,2-diaza-compounds are irradiated with ultraviolet light. For example, unsubstituted and monosubstituted indazoles (CCVII) undergo photoisomerisation under these conditions into the corresponding benzimidazoles (CCVIII).[273] The introduction of 3-phenyl-, 5-methoxy-, and 5- or 6-chloro-substituents into compounds (CCVII) inhibits the process, while an increase of temperature favours the rearrangement. A similar photoisomerisation has been observed with the unsubstituted pyrazole (CCIX), which is converted into imidazole (CCX) in 12% yield on irradiation with ultraviolet light[273]:



(CCVII) (CCVIII) (CCIX) (CCX)

The irradiation of 3-phenyl-1,2,3-benzotriazine (CCXI) sensitises the radical process, which is accompanied by the dissociation of the N–N bond and evolution of molecular hydrogen, resulting in the formation of *N*-phenylbenzazetine (CCXII):[274]



(CCXI) (CCXII)

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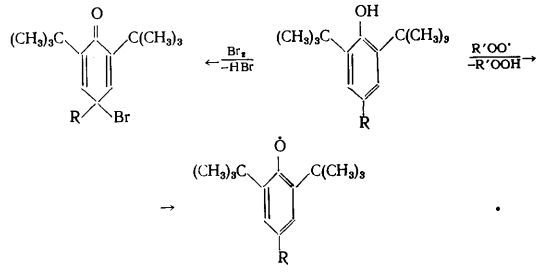
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organic reactions and of the search for ways of synthesising compounds which have not as yet been described. In connection with the high specificity of the behaviour of these compounds in reactions with one-electron transfer, it is most convenient to examine separately the properties of phenols (phenoxides), phenoxy-radicals, and cyclohexadienones in these processes.

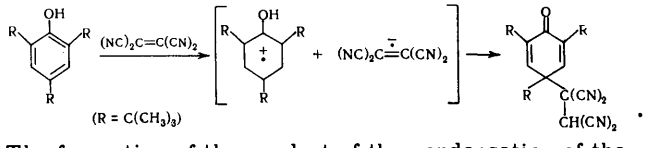
2. STERICALLY HINDERED PHENOLS (PHENOXIDES)

The hypothesis of the decisive role of the stability of the phenolic O—H bonds in reactions of sterically hindered phenols is nowadays generally accepted. It is assumed that, depending on the nature of the other reactant, the bond can be broken either homolytically[3-5] (for example in inhibited oxidation processes) or heterolytically, as in the interaction of sterically hindered phenols with electrophilic agents[6-8] (bromination, nitration and other reactions):

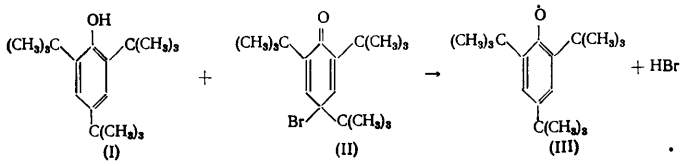


However, despite the important role of the O—H bond energy in the treatment of the mechanism of reactions of sterically hindered phenols, its value has been determined only for certain of the simplest alkylphenols[9,10].

The involvement of the hydrogen atom of the phenolic hydroxyl in the initial step in chemical reactions of sterically hindered phenols was unquestioned until recently, although there existed an alternative mechanism of this process, namely one involving reactions with transfer of one-electron. The formation of a complex, within which there is a formal possibility of the transfer of one electron has been begun to be postulated recently even for classical radical reactions such as the interaction of peroxy-radicals with sterically hindered phenols[11]. The transfer of one electron as one of the elementary steps of the chemical interaction can be postulated for reactions of sterically hindered phenols with reactants exhibiting a high electron affinity. Thus, when alkylphenols react with quinones[12] and quinolide compounds[13-15], phenoxy-radicals are formed. An analytical method for the determination of phenols is based on the reaction of sterically hindered phenols with tetracyanoethylene[16]:

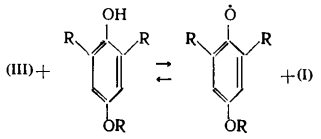


The formation of the product of the condensation of the phenol with tetracyanoethylene agrees fairly well with the possibility of the transfer of one electron in the first reaction stage. It has been shown for the reaction of 2,4,6-tri-t-butylphenol (I) with 4-bromo-2,4,6-tri-t-butylcyclohexa-2,5-dienone (II), which leads to only one product—the stable phenoxy-radical (III), that its rate is independent of the nature of the solvent and that there is no isotope effect when compound (II) is allowed to react with the phenol(I) deuterated in the phenolic hydroxyl[13]:



It follows from the kinetic data obtained for the interaction of 2,4,6-tri-t-butyl-4-nitrocyclohexa-2,5-dienone with various phenols that its activation energy depends significantly on the nature of the *para*-substituent in the phenol molecule and that it increases as the electron-accepting properties of the *para*-substituent are enhanced[15].

A typical homolytic reaction of sterically hindered phenols with phenoxy-radicals may be treated formally as a reaction in which there is an electron transfer from the phenol to the radical. If two stable radicals with approximately identical oxidation-reduction potentials are involved in this reaction, the latter is reversible[17]:



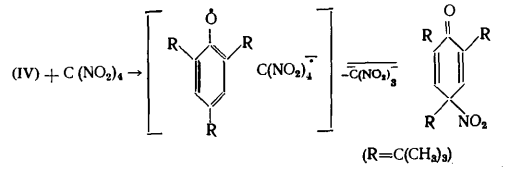
(R = C(CH$_3$)$_3$)

Studies on the transfer of a hydrogen atom between a phenol molecule and the corresponding phenoxy-radical by ^{1}H NMR have shown the possibility of the existence of an intermediate complex[18,19]. According to the views of Müller et al., this complex is an ion pair (see Section III) in which there is a transfer of one electron[20].

In contrast to sterically hindered phenols, their phenoxides have more marked electron-donating properties. For example, while the half-wave potential for the anodic oxidation of compound (I) is 1.0 V, the half-wave potential for the anodic oxidation of 2,4,6-tri-t-butylphenoxide (IV) is already in the region of zero potential[21-23]. The salts of sterically hindered phenols have been frequently used as nucleophilic components in order to confirm the hypothesis of the possibility of one-electron transfer in the interaction of two non-radical species[24-27]. Moreover, in the light of the mechanism involving one-electron transfer, the results of reactions investigated earlier, such as the oxidation of sterically hindered phenols by molecular oxygen in an alkaline medium[28-30] and the interaction of phenoxides with various reactants involving the formation of compounds characteristic of radical reactions[31,32] (the dimerisation and disproportionation products from phenoxy-radicals) become understandable.

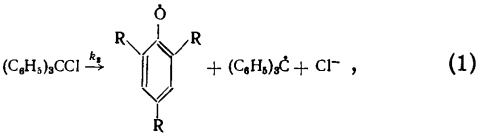
The one-electron transfer stage in the reaction between the anion and a neutral molecule has been demonstrated by the formation of a radical and the corresponding radical-anion. In the reactions of (IV) with tetracyanoethylene[33], chloranil[33], and difluorodinitromethane[24], radicals were detected by ESR:

The nitration of (IV) by tetranitromethane probably proceeds by a similar mechanism[26]:

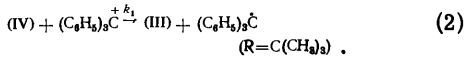


(R=C(CH$_3$)$_3$)

The study of the kinetics of the reaction of potassium 2,4,6-tri-t-butylphenoxide with chlorotriphenylmethane (trityl chloride) showed[25] that the formation of compound (III) in this case is possible via electron transfer from the phenoxide ion both to trityl chloride [reaction (1)] and to the trityl cation [reaction (2)]:



(1)



(2)

(R=C(CH$_3$)$_3$).

According to this mechanism the initial rate of accumulation of the phenoxy-radical (III) is described by the equation‡

$$W_0 = k_1'(\mathrm{TCl}) + k_2(\mathrm{TCl}) \cdot (\mathrm{ArOK})^2 .$$

The relative contribution of a particular mechanism depends significantly on the nature of the solvent. For example, an increase of the solvating capacity of the solvent leads to an increase of the contribution of reaction (2), while the reaction between the phenoxide (IV) and trityl chloride in heptane proceeds only as a trimolecular process [reaction (1)].[34] On passing from trityl chloride to trityl bromide, the rate of reaction with the phenoxide (IV) increases appreciably both via the monomolecular [reaction (2)] and the ter-molecular [reaction (1)] mechanisms. In the trityl chloride–phenoxide (IV) system, the transfer of one electron is much slower than in the reaction of trityl bromide with the phenoxide (IV), reaction (1) involving trityl bromide being 100 times faster and reaction (2) 50 times faster than the reaction of the radical (IV) with trityl chloride[35]. Tri-(*p*-nitrophenyl)methyl bromide reacts almost instantaneously with salts of sterically hindered phenols[35].

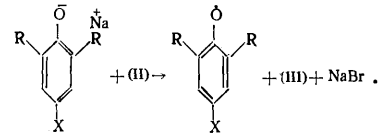
The reaction of salts of sterically hindered phenols with quinolide compounds may be regarded as a model of substitution reactions of the S_N2 type proceeding via a one-electron transfer stage[36], the activation energy of which increases in the sequence Br < Cl < NO_2 as a function of the geminal substituent in the quinolide compound. The rate of reaction depends significantly on the solvent owing to the different degrees of solvation of the metal cation by solvent molecules[36]:

$$(\mathrm{IV}) + (\mathrm{II}) \rightarrow 2(\mathrm{III}) + \mathrm{EX}$$
$$(\mathrm{X}=\mathrm{Br}, \mathrm{Cl}, \mathrm{NO_2})$$

Studies of the kinetics of the reactions of cyclohexadienone (II) (X = Br) with the sodium salts of 2,6-di-t-butylphenols containing various substituents in the *para*-position showed that, as the electron-accepting properties of the substituent become more marked, the activation energy increases and the reaction rate constant falls. This behaviour is probably related to the decrease of the effective negative charge on the oxygen atom in the phenoxide ion. The reaction does not occur with sodium 2,6-di-t-butyl-4-nitrophenoxide. The activation energy for this reaction is satisfactorily correlated with the σ_p constants of the substituents (r = 0.983; ρ = 10.2). On the other hand, this type of relation holds much less satisfactorily for the reaction rate constants[37]. The absence of a dependence of the reaction rate constants on the substituent constants may be a consequence of a compensation effect, since the pre-exponential factor for this reaction increases with activation energy (Table 1).

Table 1. Kinetic parameters of the reaction of (II) with substituted sodium 2,6-di-t-butylphenoxide in THF.

X	k (30°), litre mole^{-1} s^{-1}	k_0, litre mole^{-1} s^{-1}	E_{act} ± 0.5, kcal mole^{-1}	X	k (30°), litre mole^{-1} s^{-1}	k_0, litre mole^{-1} s^{-1}	E_{act} ± 0.5, kcal mole^{-1}
C(CH$_3$)$_3$	$5 \cdot 10^{-1}$	$4{,}7 \cdot 10^{7}$	11.0	COOC$_2$H$_5$	$2{,}5 \cdot 10^{-6}$	$3{,}6 \cdot 10^{6}$	16.9
C$_6$H$_5$	$2 \cdot 10^{-3}$	$2{,}5 \cdot 10^{5}$	11.6	COCH$_3$	$1{,}8 \cdot 10^{-5}$	$2{,}8 \cdot 10^{3}$	18.3
CHO	$2{,}4 \cdot 10^{-6}$	$8{,}0 \cdot 10^{4}$	14.5	CN	$3{,}3 \cdot 10^{-6}$	$2{,}5 \cdot 10^{5}$	19.2

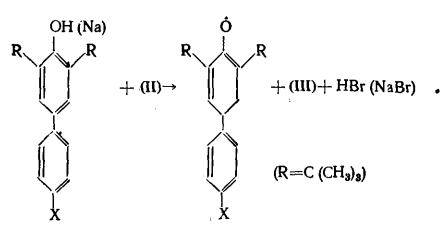


(R=C(CH$_3$)$_3$)

Comparative data for the kinetics of the reaction of (II) with 2,6-di-t-butyl-4(*p*-X-phenyl)phenols and their sodium salts have shown that the rate constants for reactions of phenols with (II) are smaller by 3–4 powers of ten than the rate constants for the analogous reactions of the corresponding phenoxide ions and the activation energies for the reactions with the phenols are almost twice as great as the energies for the reactions with their phenoxides[38] (Table 2).

Table 2. Kinetic parameters of the reaction of (II) with 2,6-di-t-butyl-4-(*p*-X-phenyl)phenols and their sodium salts in THF.

X	Phenols			Sodium phenoxides		
	$10^{8}k$, litre mole^{-1} s^{-1}	$10^{-8}k_0$, litre mole^{-1} s^{-1}	E_{act} ± 1, kcal mole^{-1}	$10^{4}k$, litre mole^{-1} s^{-1}	$10^{-5}k_0$, litre mole^{-1} s^{-1}	E_{act} ± 0.5, kcal mole^{-1}
H	2.5	0,016	19.3	1.3	3.5	11.6
C$_2$H$_5$	1.8	0.9	21.7	4.0	7.0	11.5
OCH$_3$	—	—	—	1.6	0.4	10.4
Cl	—	—	—	1.8	6.0	11.8
COCH$_3$	3.0	1.0	21.4	0.21	0.7	11.9
COOCH$_3$	2.0	2.0	22.1	0.3	11.0	10.7



(R=C(CH$_3$)$_3$)

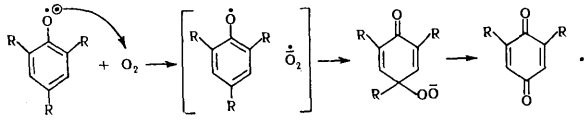
The pre-exponential factor for the reaction of (II) with sodium 2,6-di-t-butyl-4-(*p*-X-phenyl)phenoxides varies

‡ It is assumed in this equation that $k_1 > k_1'$, where k_1' is the monomolecular dissociation constant of trityl chloride.

insignificantly and for this reaction series there is satisfactory correlation between the rate constants and the σ_p constants of the substituents in the phenyl group (r = 0.994; ρ = 1.45).

Data for the reaction of sterically hindered phenols with molecular oxygen in an alkaline medium are interesting from the standpoint of one-electron transfer. The extensive factual experimental data on this question have been reviewed[39], but the mechanism of this reaction has not been discussed in detail. That it is of a radical type appears evident. During the reaction, semiquinone radicals are detected and various quinolide compounds, hydroperoxides, quinones, hydroxyquinones, and products of their further reactions are formed[39-41]. It has also been suggested[42] that the first stage in the interaction of oxygen with phenols in an alkaline medium is the formation of the phenoxy-radical.

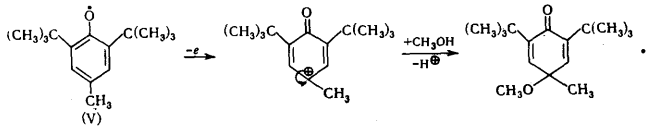
Analysis of the experimental data for the interaction of sterically hindered phenols with oxygen in an alkaline medium suggests that it does not involve a neutral molecule but the corresponding phenoxide and proceeds via a one-electron transfer mechanism. Since the phenoxy-radical and the oxygen radical-anion are formed in the "cage", the probability of their recombination increases greatly. Therefore, in the oxidation of sterically hindered phenols by atmospheric oxygen in an alkaline medium, the corresponding hydroperoxides and their decomposition products (quinones) are obtained preferentially[43,44]:



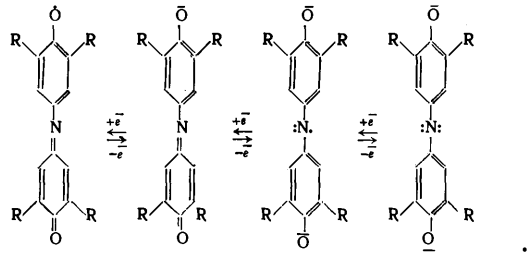
The formation of phenoxy-radicals or typical reactions products from phenoxy-radicals during the interaction of the lithium salt of 2,4,6-tri-t-butylphenol with benzenesulphenyl chloride[31] and in the interaction of potassium 2,6-di-t-butyl-4-nitrophenoxide with toluenesulphonyl chloride or chloroformate esters[32] can probably also be accounted for by one-electron transfers. It has been suggested in the literature that the reaction of salts of sterically hindered phenols with benzenediazonium chloride proceeds via a one-electron transfer stage[45].

3. STERICALLY HINDERED PHENOXY-RADICALS

In contrast to phenols, which are as a rule incapable of accepting electrons the corresponding phenoxy-radicals have distinct electron-accepting properties. Extremely unstable cations, which react in the carbonium form with the solvent, are formed as intermediates only in the anodic oxidation of certain phenoxy-radicals[21-23]. For example, the anodic oxidation of the 2,6-di-t-butyl-4-methylphenoxy-radical (V) in methanol results in the formation of 2,6-di-t-butyl-4-methoxy-4-methylcyclohexa-2,5-dienone:

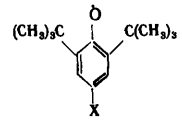


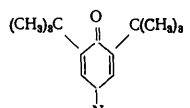
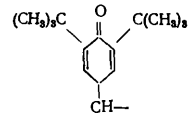
Studies on the polarographic reduction of many stable phenoxy-radicals have shown that the half-wave potentials $E'_{1/2}$ for the reduction of these radicals to the corresponding phenoxides depends on their structure and on the nature of the substituents in the phenoxy-radical (Table 3). Thus Coppinger's radical and the 2,2',6,6'-tetra-t-butylindophenoxy-radical (VI) are reduced at potentials close to zero, probably owing to the more extensive conjugation system in these radicals[46]. As a result of its structural features, the electrochemical reduction of radical (VI) entails the initial formation of a phenoxide, which is capable of accepting a further two electrons with formation of a radical-dianion and a trianion:



(VI) (R=C(CH$_3$)$_3$)

Table 3. Half-wave potentials in the polarographic reduction of the stable phenoxy-radicals[47].



X	$E'_{1/2}$, V	X	$E'_{1/2}$, V
	0.07	p-CH$_3$COC$_6$H$_4$	−0.29
		p-CH$_3$OCOC$_6$H$_4$	−0.31
		p-ClC$_6$H$_4$	−0.36
		C$_6$H$_5$	−0.37
		(CH$_3$)$_3$C	−0.38
	0.09	p-CH$_3$C$_6$H$_4$	−0.41
		p-C$_2$H$_5$C$_6$H$_4$	−0.41
p-OHCC$_6$H$_4$	−0.23	p-CH$_3$OC$_6$H$_4$	−0.45
(C$_6$H$_5$)$_3$CH	−0.28	p-(CH$_3$)$_2$NC$_6$H$_4$	−0.57

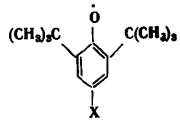
A two-electron wave ($E''_{1/2}$ = −1.4 V), which corresponds to the formation of a trianion, has been detected in the polarogram of radical (VI) in addition to the one-electron reduction wave. A similar wave has been observed in the polarographic reduction of the corresponding phenoxide. The existence of the trianion and its reversible conversion into the phenoxide ion have been demonstrated by ultraviolet spectroscopy and the intermediate formation of the radical dianion has been demonstrated by ESR.[46]

The values of $E'_{1/2}$ for 2,6-di-t-butyl-4-(p-X-phenyl)-phenoxy-radicals (Table 3) shift towards more negative potentials as the electron-donating properties of the substituent X become more pronounced and are satisfactorily correlated with the electrophilic constants σ^+ (r = 0.983). Thus, polarographic analysis shows that phenoxy-radicals are active electron acceptors and in reactions with nucleophilic agents are converted into phenoxides by

accepting one electron in a vacant orbital. Such reactions include primarily the thoroughly investigated reactions of stable phenoxy-radicals with alkali metals[48,49], phosphites[50,51], amines[2,52,53], organometallic compounds[54-57], and certain iodides[58-61]. A series of studies involving kinetic methods for the investigation of reactions of phenoxy-radicals have been made by Pokhodenko[2,49-51]. For example, he showed that the rate of reaction of triethylamine with phenoxy-radicals depends on the electron-accepting properties of the latter and that the reaction of the same phenoxy-radicals (III) with triethyl phosphite as a nucleophilic agent is much slower than that with triethylamine[50].

Comparison of the kinetic parameters for the reaction of triethylamine or diethylamine with a number of 2,6-di-t-butyl-4-(*p*-X-phenyl)phenoxy-radicals with the polarographic reduction potentials have shown that the reaction of phenoxy-radicals with tertiary amines proceeds only via the one-electron transfer mechanism (correlation of the reduction potentials of the radicals with kinetic parameters; Table 4), while in the reaction of phenoxy-radicals with secondary amines the transfer of one electron and the elimination of a hydrogen atom play a significant role simultaneously[62].

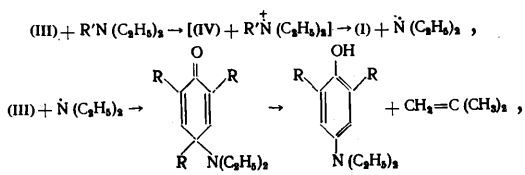
Table 4. Kinetic parameters of the re. on of the phenoxy-radicals

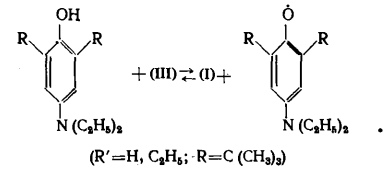


with amines.

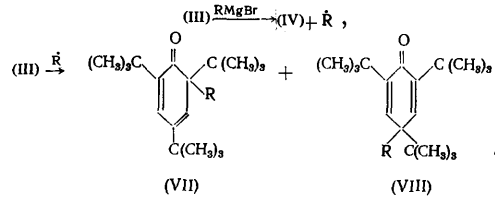
X	Triethylamine			Diethylamine		
	$10^5 k$, litre mole^{-1} s^{-1}	k_0, litre mole^{-1} s^{-1}	E_{act} ± 0.5, kcal mole^{-1}	$10^4 k_{10}$, litre mole^{-1} s^{-1}	k_0, litre mole^{-1} s^{-1}	E_{act} ± 0.5 kcal mole^{-1}
$C(CH_3)_3$	36.0	$2{,}8\cdot10^8$	12.8	9.0	$5{,}9\cdot10^5$	11.4
p-$CH_3C_6H_4$–	9,8	$3{,}7\cdot10^4$	10.7	3.8	$1{,}2\cdot10^5$	10.1
C_6H_5–	13.0	$1{,}3\cdot10^4$	10.1	10.6	$7{,}6\cdot10^4$	9.7
p-ClC_6H_4–	16.7	$7{,}3\cdot10^3$	9.5	12.5	$1{,}5\cdot10^5$	10.1
p-$CH_3OOCC_6H_4$–	25.0	$2{,}3\cdot10^3$	8.7	24.0	$4{,}0\cdot10^5$	10.3
p-$CH_3COC_6H_4$–	36.0	$3{,}9\cdot10^3$	8.8	19.6	$3{,}2\cdot10^5$	10.3

The main product of the reaction of phenoxy-radicals with amines is the corresponding phenol[62-64]. The formation of insignificant amounts of 4-*NN*-dialkylamino-2,6-di-t-butylphenoxy-radicals, detected by ESR, in the reaction of (III) with amines, shows that the interaction of the phenoxy-radical with the radical obtained from the amine takes place in the main reaction and that according to these data the overall reaction mechanism can be represented as follows:



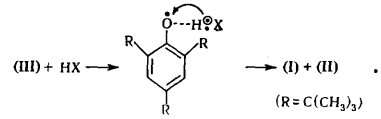


The reaction of phenoxy-radicals with organomagnesium compounds takes place almost instantaneously even at −70°C. The reaction with alkylmagnesium halides yields, apart from magnesium phenoxide, *gem*-dialkylcyclohexadienones (VII) and (VIII) owing to the interaction of the phenoxy-radicals present in excess with the alkyl radicals[57].

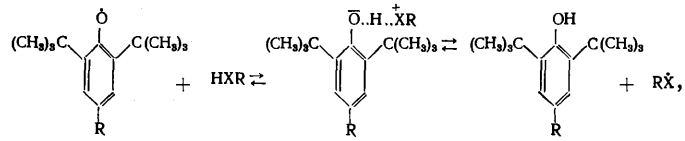


The formation of biphenyl was observed in a study of the reaction of (III) with phenyl-lithium[54] and phenylmagnesium bromide[56].

In recent years, reports have appeared in the literature in which dehydrogenation by phenoxy-radicals is regarded as involving the transfer of one electron in a complex[65-67]. This mechanism explains satisfactorily the dehydrogenation of inorganic acids by stable phenoxy-radicals[65,66,68,69], since the energy of the HX bonds in inorganic acids is as a rule higher than 100 kcal mole^{-1} [70] and therefore it is difficult to postulate the possibility of a direct elimination of a hydrogen atom from such a substrate by a phenoxy-radical:



Müller et al., who investigated a large number of reactions involving dehydrogenation by phenoxy-radicals, postulate the formation in the first stage of an ion pair complex in which one-electron transfer can take place[20]:



where X = heteroatom.

Among reactions of a similar type, the dehydrogenation of various phenolic compounds and amines by phenoxy-radicals has been most completely studied[71-76]. Although the investigators of these reactions in most cases supported the mechanism where atomic hydrogen is eliminated in the elementary step, nonetheless their experimental data fits satisfactorily the hypothesis of the one-electron transfer mechanism for the process.

4. STERICALLY HINDERED CYCLOHEXADIENONES

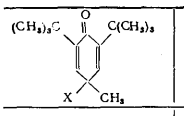
The factor which determines the reactivity of various cyclohexadienones (quinolide compounds) is the nature of the geminal substituents, which in many ways determines

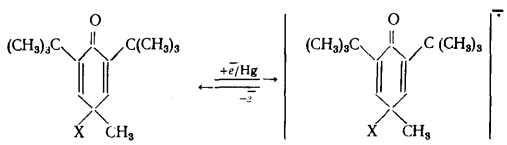
the specificity of the chemical behaviour of the molecule and in the first place its tendency to undergo reactions with a one-electron transfer (reactions with nucleophilic agents and metals and electrochemical reduction). The effect of the nature of the geminal substituents on similar process has been shown most distinctly in the polarographic reduction of quinolide compounds[77].

Electron affinity (the energy of the lowest vacant molecular orbital[78]) is usually satisfactorily correlated with the half-wave potential for the polarographic reduction of the quinolide compound in aprotic media. Therefore polarographic reduction data for quinolide compounds can be used as indices of the reactivity of these compounds in their interaction with the electron, which is the simplest nucleophilic agent.

The polarographic reduction of 4-alkyl-2,6-di-t-butyl-4-methyl-cyclohexa-2,5-dienones (VIII) and (IX) at a dropping mercury electrode in dimethylformamide solution (DMF) gives rise to a one-electron wave, the analysis of which indicates the reversibility of the process occurring in the reduction of compounds (VIII) and (IX) (Table 5).[77]

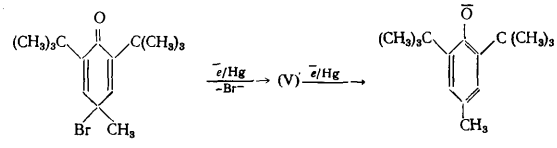
Table 5. Polarographic characteristics of quinolide compounds.

	$E'_{1/2}$, V	i_d, μA	α	$E''_{1/2}$, V	i_d, μA	α
Br	—0.31	1.0	1.0	—0.46	0.52	0.4
Cl	—1.13	3.05	0.9	—	—	—
NO_2	—1.30	3.13	0.8	—	—	—
OCH_3	—1.31	1.66	0.6	—2.20	0.36	0.8
OH	—1.59	1.44	0.2	—2.18	0.54	0.8
CH_3	—2.18	1.48	1.0	—	—	—
$C(CH_3)_3$	—2.24	1.82	1.0	—	—	—



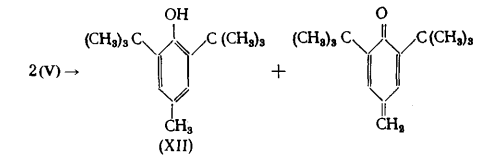
X=C(CH₃)₃ (VIII) X=C(CH₃)₃ (VIIIa)
X=CH₃ (IX) X=CH₃ (IXa)

The formation of the radical-anions (VIIIa) and (IXa) has been confirmed by ESR (the spectrum of the radical-anion consists of a 1:2:1 triplet, $a_{H(meta)}$ = 6.6 G).[79] The polarographic reduction of the quinobromide (X) gives rise to two polarographic waves:



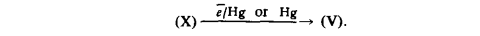
(X) (XI)

At the first half-wave potential ($E'_{\frac{1}{2}}$ = −0.31 V), the phenoxy-radical is formed instead of the corresponding radical-anion which indicates the dissociation of the C—Br bond in the electrochemical reduction process with formation of the phenoxy-radical and a bromide ion[77,79]. The second one-electron wave is due to the reduction of (V) and is irreversible. The limiting current of the second half-wave for the polarographic reduction of the quinobromide (X) was found to be lower than would be expected for a one-electron process and is probably related to the simultaneous disproportionation of the phenoxy-radical via the mechanism[80]:



(XII)

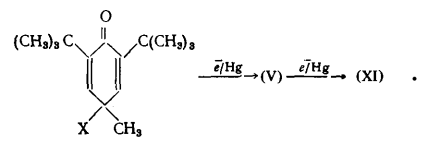
It is noteworthy that quinobromides react slowly with neutral mercury[48], forming phenoxy-radicals and this is why the limiting current for the polarographic reduction of the quinobromide (X) seems to be low, (i_d = 1 μA instead of i_d = 1.5 ± 0.2 μA for the one-electron process):



These two simultaneous processes involve the same mechanism but proceed at different rates. The initial stage is electron transfer in both cases.

The polarographic reduction of quinobromides, where the bromine atom is linked to a tertiary carbon atom, constitutes a specific example of the polarographic reduction of alkyl halides. Usually the electrochemical reduction of tertiary alkyl halides has a low transfer coefficient, since the reduction of these compounds has a S_N1-like mechanism[81]. In the polarographic reduction of compound (X), the transfer coefficient α = 1, which may indicate electron transfer from the cathode directly to the vacant orbital of the bromine atom in the molecule of (X).

The quinochloride (XIII) and the 4-nitrocyclohexadienone (XIV) interact with an electron at more negative potentials than (X) and (V). In these cases, one two-electron wave due to the stage-by-stage one-electron reduction is observed in the polarographic reduction process[77]:

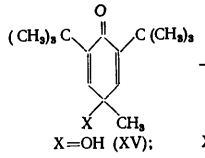


X=Cl (XIII); X=NO₂ (XIV)

The intermediate formation of a phenoxy-radical in a similar electrochemical reaction has been confirmed by ESR.[82]

Analysis of the results of the polarographic reduction of hydroquinone (XV) and its methyl ether (XVI) showed that the mechanism of their reduction differs from that described above. The difference consists primarily in the fact that the main (first) polarographic wave corresponds to a one-electron process. This rules out the intermediate formation of a phenoxy-radical as the main reaction product, since the reduction potentials of (XV) and (XVI) are more negative than the reduction potentials of (V) and other phenoxy-radicals[46]. In addition, the transfer coefficient in the polarographic reduction of (XV) and (XVI) differs markedly from the transfer coefficient for the first polarographic wave of (X), probably because of the decrease of the transfer of a fractional electronic charge in the transition state in the reduction of (XV) and (XVI). It is most likely that electron capture by hydroquinone (XV) or its ether (XVI) leads to the formation of

the corresponding phenoxide (with simultaneous elimination of the radicals $\dot{O}H$ or $\dot{O}CH_3$) and not of a phenoxy-radical and an anion:



$\xrightarrow{\bar{e}/Hg}$ (XI) + $\dot{X}$.

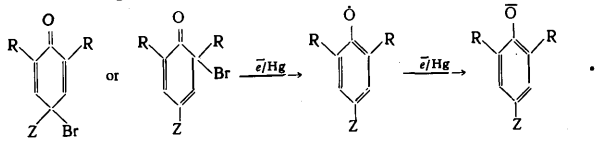
X=OH (XV); X=OCH_3 (XVI)

According to this mechanism of the polarographic reduction of (XV) and (XVI), the formation of a second wave ($E''_{1/2} \simeq -2.19$ V), the limiting current of which is smaller almost by a factor of three than that of the first wave, may be attributed to the reduction of substances produced from the solvent when it interacts with the radicals $\dot{O}H$ and $\dot{O}CH_3$ (Table 5).

Table 6. Polarographic characteristics of quinobromides.

Position of bromine atom	Z	$E'_{1/2}$, V	i_d, μA	α	$E''_{1/2}$, V	i_d, μA	α
4	CH_2Br	—0.24	1.0	1.0	—0.39	1.0	0.9
2	CHO	—0.13	1.7	0.4	—0.42	1.4	0.4
2	$COCH_3$	—0.11	1.4	0.7	—0.47	1.5	0.4
2	CN	—0.01	1.0	0.6	—0.[illegible]	1.1	0.4
2	Br	0.05	0.9	0.8	—0.[illegible]	1.5	0.8
2	NO_2	0.13	1.0	0.3	—0.29	1.0	0.7

The introduction of a second functional group into quinolide compounds has a significant influence on the results of their polarographic reduction. Interesting data were obtained in the reduction of quinobromides with various substituents in the 4-position[77] (Table 6). In such cases, two one-electron waves are produced, corresponding to the individual stages of the reduction process occurring at different potentials. The first stage proceeds with transfer of one electron from the cathode to the quinobromide molecule, the reaction being accompanied by the formation of a phenoxy-radical and a bromide ion. The second stage is the reduction of the phenoxy-radical:



(Z=CH_3, CH_2Br; Br; CHO; $COCH_3$; CN; NO_2 R=C $(CH_3)_3$)

The electron affinity (the first half-wave potential) of substituted quinobromide compounds increases with increase of the negative inductive effect of the substituent.

The limiting current depends significantly on the nature of the substituent in the quinobromides and on the properties of the intermediate phenoxy-radicals. The dependence of the transfer coefficient on the solvent for quinobromide compounds indicate a significant contribution of the electronic effects of these substituents to the transition state. However, despite the fact that in the polarographic reduction of many quinobromides compounds the transfer coefficient changes and in addition the electrochemical reaction is accompanied by a chemical reaction, the calculated first half-wave potential for the polarographic reduction of quinobromides compounds are satisfactorily correlated with Taft's σ constants ($r = 0.952$). The presence of such correlation may serve as confirmation of the generality of the mechanism of the electrochemical reduction of quinobromide compounds. Probably the electron cloud of the bromine atom shifts under the influence of electronegative substituents, the atom requiring as a result a positive charge. In the electrochemical reduction, an electron is transferred to a vacant bromine orbital and more readily the higher the partial positive charge on the bromine atom. The elimination of a bromide ion with a formal homolytic dissociation of the C—Br bond in the quinolide compound molecule is a consequence of the electron transfer. The mechanism proposed for the interaction of quinolide compounds with an electron is satisfactorily consistent with experimental polarographic data and is fully consistent with the reactions of the various quinolide compounds involving one-electron transfer.

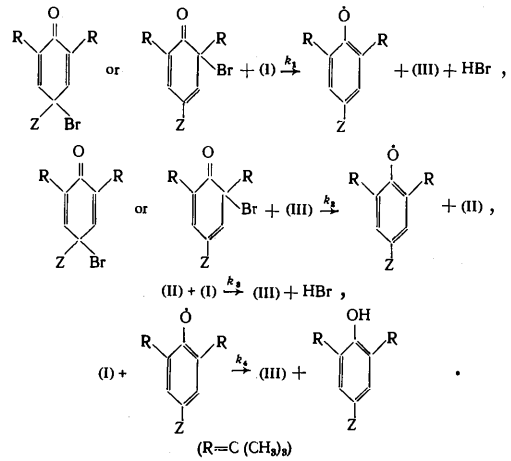
It has been found from kinetic data[83] for the reaction of (III) with hydrogen halides and the phenolic OH and halogen bond energies that $E_{C-Br} = 16.6 \pm 3$ kcal mole^{-1} and $E_{C-Cl} = 32.9 \pm 3$ kcal mole^{-1} for quinohalides:

2(III) + HX $\rightleftarrows$ (I) + (II) .

The unusually low bond energies between the halogen atom and a carbon atom of the six-membered ring of cyclohexadienones make quinobromides and quinochlorides compounds (as well as 4-nitrocyclohexadienones) thermally unstable, the compounds decomposing even at temperatures below 100°C with formation of phenoxy-radicals[58,84,85]. For this reason, certain quinobromides rearrange spontaneously on standing at room temperature to 3,5-di-alkyl-4-hydroxybenzyl bromides[85,86]. The reaction involves the intermediate formation of a phenoxy-radical.

A kinetic study of the interaction of various quinobromides with (III) has shown that the activation energy increases with the electronegativity of the substituent in the quinobromide[87]. This relation indicates an increase of the resistance of the C—Br bond to homolytic dissociation in the series of bromocyclohexadienones with increase of the electronegativity of the substituent (Table 7).

An analogous relation has been obtained in a kinetic study of the reaction of the same quinobromides with (I),[14] although the reaction does not stop in the first stage. In the presence of an excess of the quinobromide, the four reactions represented in the scheme below can occur:



(R=C $(CH_3)_3$)

In the reaction with a quinobromide containing the nitro-group (Z = NO_2), $k_1 = 7 \times 10^{-6}$, $k_2 = 8 \times 10^{-2}$, $k_3 = 5 \times 10^{-7}$, $k_4 = 10^3$ litre mole^{-1} s^{-1}.

gem-Dialkylcyclohexadienones, hydroquinones, and their ethers are as a rule more thermostable and therefore the bond energy between the geminal substituent and a carbon atom in the six-membered ring presumably differs little from the C—C or COR bond energy in the usual organic compounds. Consequently the properties of quinolide compounds change sharply on passing from quinobromide, quinochloride, and 4-nitrocyclohexadienones to other cyclohexadienones. Their behaviour in reactions with one-electron transfer is determined by the lower electron affinity of the geminal substituent and the higher stability of the bond linking it. Thus the reaction of *gem*-dialkylcyclohexadienones with metallic potassium in tetrahydrofuran yields a stable radical-anion[79]:

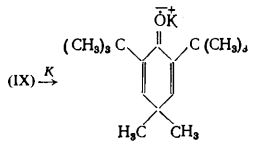
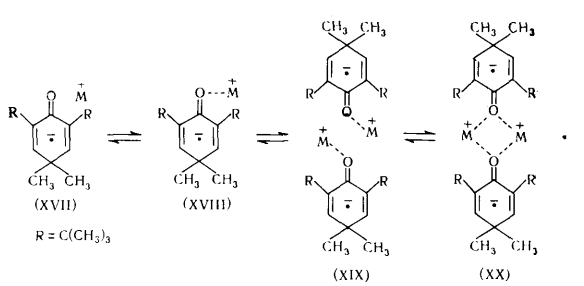


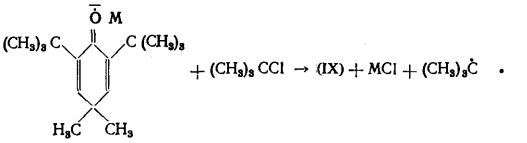
Table 7. Activation energies for the reaction of (III) with bromocyclohexadienones.

Z	Position of bromine atom	$E_{act} \pm 1$, kcal mole^{-1}	Z	Position of bromine atom	$E_{act} \pm 1$, kcal mole^{-1}
CH_3	4	4.2	CHO	2	13.1
CH_2Br	4	7.0	Br	2	13.7
CN	2	12.4	NO_2	2	13.2

The structure of the paramagnetic species obtained in the interaction of *gem*-dialkylcyclohexadienones with alkali metals depends significantly on the nature of the metal, the solvent, and temperature. A detailed analysis of the ESR spectra of the radical-anions from the cyclohexadienone (VIII), obtained in different media, made it possible to deduce the chain of reactions involving these radical-anions when the solvating capacity of the solvent is reduced[88]:



The ion pair (XVII) separated by solvent molecules is converted into a contact ion pair (XVIII) which is subsequently converted into the paramagnetic dimer (XIX) separated by solvent molecules. In turn, the dimer (XIX) is converted into a contact dimer (XX). It has been shown[88-91] that the cations are desolvated in the course of these transformations. It has been established for the reaction of the above radical-anions with t-butyl chloride[92], the rate-limiting stage of which is apparently the transfer of one electron from the radical-anion to the alkyl halide, that the reactivity of the radical-anion increases with decrease of the degree of desolvation of the cation:

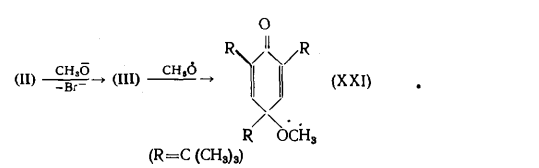


The activation energy for this reaction is higher in solvating media and increases in the series of cations TBA§ < Na < Li (Table 8). The formation of metal chlorides is accompanied by the disruption of the solvation shell of the cation and presumably the differences between the activation energies are related to the difference between the heats of solvation of the corresponding cations. Indeed, the difference between the activation energies in THF and in ethyl ether for the reaction of t-butyl chloride with the radical-anion of 2,6-di-t-butyl-4,4-dimethylcyclohexa-2,5-dienone, with Na^+ and Li^+ as the cations, is the same as the difference between the heats of solvation of these cations by the solvent molecules, calculated by analysing the ESR spectra of the radical-anions[88-92].

Table 8. Kinetic parameters of the reaction of t-butyl chloride with the radical anion of the metal derivative of 2,6-di-t-butyl-4,4-dimethylcyclohexa-2,5-dienone.

Cation	Solvent	$10^3 k$ (0°), litre mole^{-1} s^{-1}	$10^{-10} k_0$, kcal mole^{-1} s^{-1}	$E_{act} \pm 0.5$, kcal mole^{-1}
Sodium	DME	0.79	0.4	15.6
Sodium	THF	1.50	2.4	16.3
Sodium	Ethyl ether	7.00	0.1	13.5
Lithium	THF	0.09	260	20.4
Lithium	Ethyl ether	0.40	0.04	14.7
TBA	THF	$5 \cdot 10^2$	0.1	11.3

All the data quoted above show that, among quinolides of different types, the quinobromides should enter most readily into chemical reactions involving the transfer of one electron. Indeed, reactions of this type proved to be extremely characteristic of such compounds. The majority of known reactions of quinobromides, for which an ionic mechanism has been postulated earlier, probably proceed via the scheme under consideration. For example, 2,4,6-tri-t-butyl-4-methoxyhexa-2,5-dienone (XXI) was obtained in the reaction between compound (II) and alkaline solutions of methanol and the appearance of a blue colour in the course of the reaction was noted[48]. Only later was it shown that the blue colour is due to the appearance of the phenoxy-radical (III):[93]



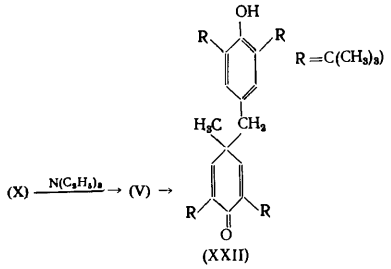
The phenoxy-radical (X) is also formed when compound (II) interacts with amines[93-96], organomagnesium compounds[97], alkyl phosphites[50,51], triphenylphosphine[98], phenoxides[36-38,48,99], and various metals[48,49,54,58].

§ TBA = tetrabutylammonium.

Certain metals, such as mercury, silver, copper and zinc, are readily oxidised on reacting with quinobromides and only the phenoxy-radical is obtained from compound (II).[48] The radical (III) is also formed initially by the reaction of compound (II) with alkali metal and is capable of further reaction with these electron donors, so that the final product is the corresponding phenoxide[48,49]:

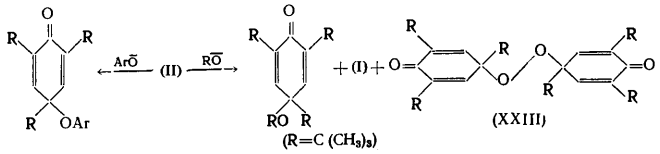
$$(III) \xleftarrow[95\%]{Ag} (II) \xrightarrow{K} (III) \xrightarrow{K} (IV).$$

The nature of the products of the reaction of quinobromides with nucleophilic agents depends significantly on the nature of the substituents in the quinobromide molecule and on the stability of the phenoxy-radicals formed. If unstable phenoxy-radicals are obtained in the reaction of quinobromides with nucleophilic agents, then a considerable amount of products of the recombination and disproportionation of the phenoxy-radicals are present in the reaction mixture[100-103]. Therefore reaction conditions have a significant influence on the results of the interaction of the same reactants. For example, at room temperature the quinobromide (X) reacts very slowly with triethylamine and therefore it has been stated[104] that it is stable in relation to triethylamine. However, at an elevated temperature the reaction of (X) with triethylamine and certain other amines is fairly vigorous and involves the formation of the quinolide compound (XXII) as the main product[95]:



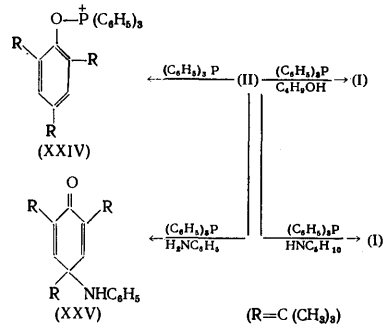
(XXII)

The reaction of compound (II) with phenoxides leads to the formation of hydroquinone ethers in almost quantitative yields[105,106], but in the reaction with alkoxides (particularly at a reduced temperature) compound (I) and the quinolide peroxide (XXIII) are also formed in considerable amounts owing to the interaction of the radical (III) with oxygen[93]:



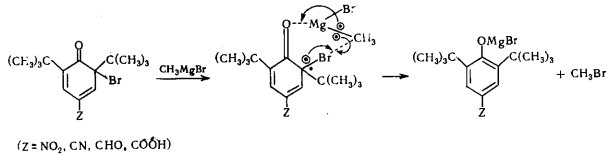
(R=C(CH3)3) (XXIII)

It is interesting that the hydroquinone ether (XVI) is also produced as a result of the interaction of the quinobromide (X) with methanol[107]. The effect of the solvent and other factors have been investigated in the reaction of compound (II) with triphenylphosphine[98]. The radical (III) is also formed initially in this reaction and then reacts further with formation of the substances indicated below:



When the reaction is carried out in the absence of a solvent, the triphenylphosphine derivatives of 2,4,6-tri-t-butylphenol (XXIV) is formed, in solution in s-butyl alcohol or piperidine the product is compound (I), and in the presence of aniline the quinamine (XXV) is isolated. There is now no doubt about the radical mechanism of the reaction of quinobromides with alkyl phosphites[50,51], although initially an ionic mechanism was proposed for this reaction[108,109].

Interesting data were obtained also in a study of the reaction of quinobromides with organomagnesium compounds. Firstly, it was shown in this reaction that organomagnesium compounds can take part in reactions involving the transfer of one electron and, secondly, it was possible to elucidate the effect of the nature of the substituents in the quinobromide molecule on the properties of the bromine atom in chemical reactions involving the transfer of one electron. It was found that, depending on the nature of the substituents in the quinobromides, their reaction with a Grignard reagent results in the formation of either a magnesium halide and a phenoxy-radical or of an alkyl bromide and the corresponding phenoxide ion[110]. The second reaction pathway is possible for quinobromides containing electronegative substituents. Such quinobromides usually have an *ortho*-quinolide bond system[111]. It is noteworthy that in this case electronegative substituents enhance the electron affinity of the quinobromides to an even greater extent (see, for example, the data for their polarographic reduction in Table 6). To account for this reaction pathway, it has been suggested that the C—Br bond in quinobromides becomes more heteropolar under the influence of electronegative substituents than the corresponding bond in analogous compounds with alkyl substituents only[112]. Therefore, the transfer of one electron in the reaction of the above quinobromides with a Grignard reagent make more favourable the formation of a phenoxide ion (stabilised by internal conjugation) with the formal elimination of bromine in the form of a radical rather than the formation of a phenoxy-radical:



(Z = NO2, CN, CHO, COOH)

The same mechanism has been proposed also for the reaction of certain α-bromoketones with metal carbonyls and the formation of the bromine radical was confirmed experimentally[113]. It is interesting that an analogous reaction mechanism holds also in the interaction of organomagnesium compounds with cyclohexadienones in which one of the geminal substituents is the OH or OCH_3 group. These reactions yield only phenoxides[114]. Thus butyl methyl ether was isolated in addition to compound (XII) in the reaction of (XVI) with butylmagnesium bromide:

$$(XVI) + C_4H_9MgBr \rightarrow (XII) + C_4H_9OCH_3 .$$

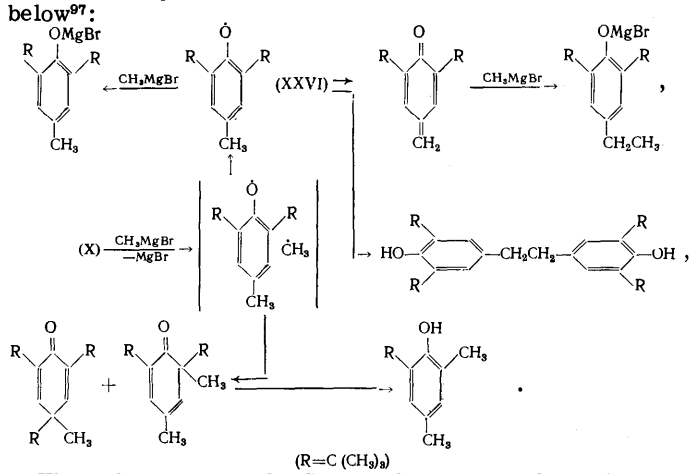
gem-Dialkylcyclohexadienones are stable also in the presence of an excess of the Grignard reagent and form radical-anions, which are reconverted into quinolide compounds in the presence of acid.

In a study of the above reactions of quinobromides with electron-donating agents accompanied by the formation of two radicals and the elimination of a bromide ion, account must undoubtedly be taken of the formation of a biradical "cage" and of the effects of its properties on the further reaction pathway. Hypotheses concerning the "cage" effect in radical reactions, in particular in reactions with one-electron transfer, are now being developed and have been generally accepted[115-117]. Depending on the properties of the "cage", determined by various factors, two processes are possible under these conditions. Firstly, radicals forming the "cage" may recombine within the "cage", yielding the expected reaction product. Secondly, on overcoming the solvation shell the radicals become kinetically independent species and as a rule give rise to a large number of side products in addition to the main reaction product. Usually these two processes are competitive. In the vast majority of cases, they take place simultaneously in reactions of quinolide compounds with one electron transfer, but their probabilities are different (depending on the nature of the nucleophilic agent, the solvent, temperature, and even the order in which the reactants are added). For example, the order of addition of the reactants in the reaction of quinobromides of types (II) or (X) with a Grignard reagent has a very significant influence on the results of the reaction.

Table 9. Rate constants for the reaction of (X) with amines at 40°C.[118]

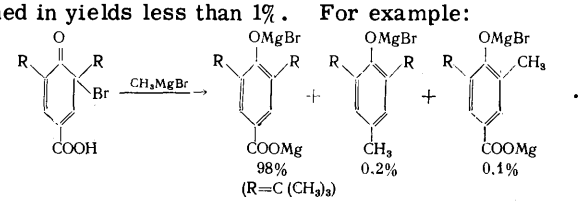
Amine	Solvent	10^3k, litre mole^{-1} min^{-1}	Amine	Solvent	10^3k, litre mole^{-1} min^{-1}
Morpholine	CCl_4	6.1	Di-isopropyl amine	Benzene	2.3
ditto	Heptane	5.5	t-butylamine	ditto	0.4
»	Benzene	6.1	Diethylamine	»	19.0
»	THF	15.0	Triethylamine	»	45.0
»	Dioxan	18.0	Piperidine	»	43.0

When an ethereal solution of (X) is added to a Grignard reagent, the phenoxy-radical (XXVI) is mainly formed and is consumed both in the disproportionation reaction and in the interaction with an excess of the organomagnesium compound. When the reactants are added in the opposite order, up to 20–30% of *ortho*- and *para-gem*-dialkylcyclohexadienones is formed in addition to compound (XXVI) and the products of its further reactions, part of the cyclohexadienones being formed as a result of the recombination of radicals within the "cage". The overall result of the secondary reactions of (X) with methylmagnesium bromide is the formation of seven different compounds via the mechanisms illustrated below[97]:



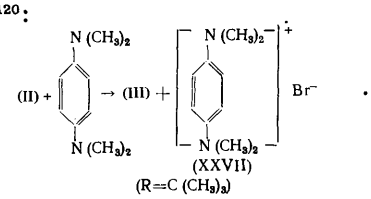
(R=C(CH$_3$)$_3$)

When the reaction of a Grignard reagent with a quinobromide containing electronegative substituents is carried out, the order of addition of the reactants no longer has a significant influence on the nature of the reaction products, since the transfer of one electron results in the preferential formation of the corresponding phenoxide and only a slight amount of phenoxy-radicals, which have been detected by ESR.[110] Therefore the products of the recombination of these phenoxy-radicals with alkyl radicals are formed in yields less than 1%. For example:



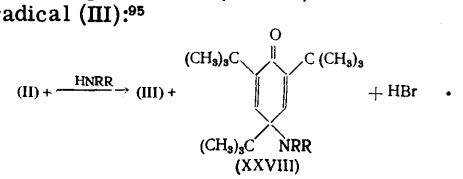
(R=C(CH$_3$)$_3$)

The effect of the "cage" on the nature of the products has been investigated also in the reaction of quinobromides with amines[118-120]. In a study of the reaction of (II) with tetramethyl-*p*-phenylenediamine by ESR, it was shown that the formation of (III) and the amine radical-cation (XXVII) is quantitative[120]:



(R=C(CH$_3$)$_3$)

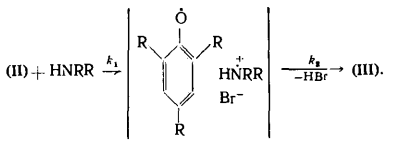
On the other hand, in the reaction of (II) with morpholine and piperidine products of the substitution of bromine by an amine—the quinamines (XXVIII)—are formed in addition to the radical (III):[95]



It follows from the kinetic data obtained for the consumption of the initial quinobromide and the accumulation of the phenoxy-radicals that the reaction is bimolecular and is of first order with respect to the quinobromide and the amine. The rate constant for the reaction of (X) with morpholine increases only slightly with the solvating capacity of the solvent, but the rate of the reaction of the same quinobromide depends significantly on the nature of the amine (Table 9). It has been shown for the reaction of (X) with

diethylamine and its *N*-deuteriated analogue that there is no isotopic effect in this process.[118]

On the hypothesis of one-electron transfer, the mechanism of the initial reaction step can be represented as follows:



The amine radical-cation formed in this step readily split off a proton and is converted into an amine radical. The latter either recombines in the "cage" with a phenoxy-radical, which leads to the main reaction product (quinamine), or emerges from the "cage" to give other reaction products. Its liberation from the "cage" is accompanied by the accumulation of phenoxy-radicals. Bearing in mind that only phenoxy-radicals emerging from the "cage" with a probability φ are detected, according to the proposed mechanism the rate of accumulation of the amine hydrobromide and phenoxy-radicals can be formulated as follows: $d[\dot{PhO}]/dt = k_2[PhOBr]$, $d[HBr]/dt = k_1[PhOBr]$, and $k_2 = \varphi k_1$, where [PhOBr] is the concentration of the quinobromide, [PhO˙] the concentration of phenoxy-radicals, [HBr] the concentration of hydrogen bromide, and φ the fraction of radicals released from the "cage".

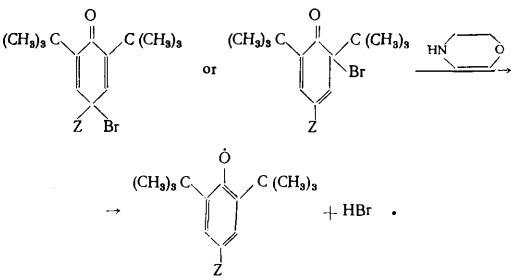
Table 10. Kinetic parameters of the reaction of (II) with amines and yields of quinamines.

Method	Amine	k_1 (40°), litre mole^{-1} min^{-1}	$10^4 k_2$ (40°) litre mole^{-1} min^{-1}	$10^{-8}k_0$, litre mole^{-1} min^{-1}	$1-\varphi$*	Yield of quinamine, %
Accumulation of HBr	Morpholine	28	—	0.8	0.93	85
Accumulation of (III)	Morpholine	—	1.9	0.72		
Accumulation of HBr	Piperidine	18	—	7.0	0.33	12
Accumulation of (III)	Piperidine	—	12	12.0		

* $1 - \varphi$ is the fraction of radicals (III) recombining within the "cage".

The kinetics of the accumulation of both hydrogen bromide (amine hydrobromide) and of radicals (III) have been investigated for the reaction of compound (II) with morpholine and piperidine[118]. The fraction of radicals released from the "cage" was calculated from the constants obtained for the formation of the "cage" and the liberation of radicals from the "cage" (Table 10). The kinetic data for this reaction were found to be in good agreement with the corresponding experimental results. Thus the reaction of (II) with morpholine yields 85% of the quinamine [2,4,6-tri-t-butyl-4-(*N*-morpholinyl)hexa-2,5-dienone]. Analysis of the kinetics of this reaction showed that the yield of the quinamine is 93%. On the other hand in the reaction of (II) with piperidine, the main pathway involves the liberation of radicals from the "cage" and therefore the rate constants found by the two methods agreed to within 30%. These results may be regarded as one of the pieces of evidence in support of the proposed mechanism involving the transfer of one electron in the elementary step of the interaction between two neutral substances.

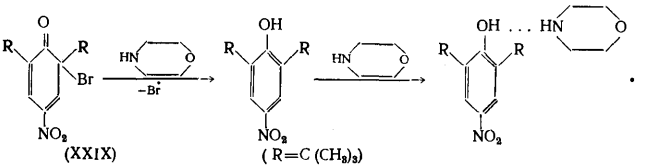
Additional data confirming the hypothesis of the one-electron stage were obtained in a study of the kinetics of the reaction of a number of quinobromides with an amine; depending on the nature of the substituents in the quinobromide molecule, the number of phenoxy-radicals liberated from the "cage" varied within wide limits[119]. Nevertheless the logarithms of the rate constants in this reaction series fit with a satisfactory correlation (r = 0.984) the relation with the first half-wave potential in the polarographic reduction of quinobromides. A similar relation, with a correlation coefficient r = 0.993 was established between the logarithms of the rate constants for the reaction of morpholine with quinobromides and Taft's constants σ for the substituents in the quinobromide molecule. It follows from these results that the effect of substituents in the reaction series investigated mainly involves an inductive mechanism:



(Z=CH$_3$; C$_2$H$_5$; C(CH$_3$)$_3$; CH$_2$Br; COCH$_3$; Br)

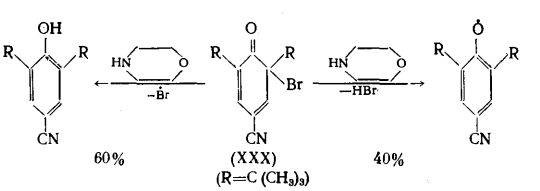
When the reaction of morpholine with quinobromides containing functional substituents was carried out, the corresponding quinamines could not be isolated, which is evidence of the preferential liberation of radicals from the "cage" under these conditions[119]. The phenoxy-radicals formed in this instance are consumed mainly via two pathways; in the reaction with the amine with formation of the phenoxide anion and in the disproportionation reaction[100].

It is noteworthy that the reaction of morpholine with the quinobromides (XXIX) and (XXX), where the substituents are nitro- and cyano-group, takes place somewhat differently. For example, in the reaction of morpholine with (XXIX) (Z = NO$_2$), the formation of hydrogen bromide and of the phenoxy-radical is not observed and the reaction yields only 2,6-di-t-butyl-4-nitrophenol which forms a complex in the presence of an excess of the amine[119]:



(XXIX) (R=C(CH$_3$)$_3$)

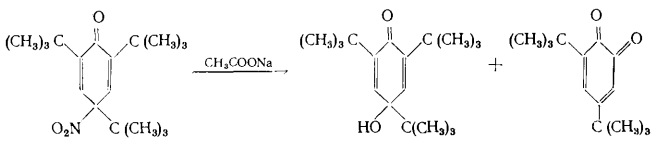
About 60% of hydrogen bromide is formed in the reaction of morpholine with (XXX) (Z = CN), which is evidence of the occurrence of approximately equivalent pathways in the decomposition of the hypothetical radical-anion with formation of both the bromide ion and atomic bromine:



60% (XXX) (R=C(CH$_3$)$_3$) 40%

These results are satisfactorily consistent with the behaviour of the above cyclohexadienones in their reactions with organomagnesium compounds[112].

The general characteristics of the reactions of quinochloride compounds and 4-nitrocyclohexadienones with nucleophilic agents remain the same as those of the reactions with quinobromide compounds, but these types of quinolides have been much less thoroughly investigated. Thus, it is known that the reaction of quinochlorides and 4-nitrocyclohexadienones with metals[48,49,54], phosphites[50,51], amines[2], and organometallic compounds[114] results in the formation of phenoxy-radicals. When potassium iodide acts on quinochlorides, free iodine is liberated[121] while in the reaction of 4-nitrocyclohexadienones and quinochlorides in aqueous alcoholic solutions of alkali, phenoxy-radicals are also formed initially[49]. The final product of the reaction of 2,4,6-tri-t-butyl-4-nitrocyclohexa-2,5-dienone with alkali (in aqueous acetone solution) is the corresponding hydroquinone[60]. It is interesting that the analogous reaction involving the replacement of the nitro-group by a hydroxyl takes place also under the influence of sodium acetate in acetic acid solution[60,122,123]:



We believe that the mechanism proposed for this reaction and involving nucleophilic substitution[122] is doubtful, since the hydrolysis of 4-nitrocyclohexadienones results in the formation, apart from the hydroquinones indicated above, of products characteristic of reactions in an alkaline medium of the corresponding phenoxy-radicals; quinones, 3,5-di-t-butyl-4-hydroxybenzaldehyde, and others[122,123] (see also Refs. 33–42).

Hydroquinones, their ethers, and *gem*-dialkylcyclohexadienones are as a rule resistant to the reaction of the majority of nucleophilic agents and only active electron donors such as alkali metals (or others in electrochemical reduction) can react with these quinolides to form radical-anions[79]. Examples of reactions of hydroquinones involving the carbonyl group are also known. Thus the reaction of 2,6-di-t-butyl-4-hydroxy-4-methylcyclohexa-2,5-dienone with organolithium compounds results in the formation of the corresponding cyclohexadienediols[124].

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The reactions of sterically hindered phenols and their derivatives discussed above are in many cases typical for substances of this type and probably involve one-electron transfer in the elementary step. Quinobromide compounds, which form either phenoxy-radicals or the corresponding phenoxides after the addition of the electron depending on the structure, are of greatest interest for the investigation of various aspects of the problem under consideration. This makes it possible to separate the various stages in processes involving one-electron transfer.

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Institute of Chemical Physics,
USSR Academy of Sciences,
Moscow

Institute of Organic
Derivatives of the Elements,
USSR Academy of Sciences,
Moscow

U.D.C. 541.183.12

Thermal Stability of Anion-exchange Resins

P.E.Tulupov and N.G.Polyanskii

This paper is a logical continuation of the previous review by the authors[1] and reflects the present state of studies on the thermal stability of anion-exchange materials. It deals with the principal methods for the investigation of the thermal stability of anion-exchange resins and presents rational formulae for the recalculation of exchange capacities which facilitate comparison of the experimental data of different investigators. Attention has been concentrated on a general description of data on the thermal stability of different anion-exchange resins in air, in water and aqueous solutions, and in organic and mixed media. A new mechanism is proposed for processes involving changes in ion-exchange resins in the above media. Rigorous kinetic equations describing the decrease of the exchange capacity with respect to highly basic groups, deamination, and degradation of the amino-groups in anion-exchange resins have been obtained on its basis and agree satisfactorily with the experimental data. Further aims of studies on the thermal stability of ion-exchange resins have been outlined.
The bibliography includes 112 references.

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I. INTRODUCTION

Anion-exchange resins, like cation-exchange resins, are in practice frequently subjected to heat treatment. In many cases heating accompanies even the preliminary preparation of the anion exchangers for experiments in order to remove as far as possible trapped water or another solvent. Some investigators dry anion-exchange resins in air[2], others *in vacuo* at 64°C, and yet another group use a thermostat at 100°C.[3,4] Regardless of the drying conditions, strongly basic anion-exchange resins undergo far-reaching chemical changes[5].

Anion-exchange resins are frequently employed at an elevated temperature for the analytical separation of multicomponent mixtures[6] but for the usual single employment of the sorbent the problems of durability have of course not been considered.

On the other hand, in catalysis by ion-exchange resins[7] durability is of prime importance, determining the possibility of reusing the catalyst and frequently deciding whether its employment is economical.

Water treatment undertakings are the largest consumers of anion-exchange resins (together with cation-exchange resins) and for these purposes the thermal stability of these high-polymer electrolytes determines not only whether or not the technological processes are economical but also the quality of the deionised water[8,9].

Despite the enormous theoretical and practical importance of this problem,the number of studies on the thermal stability of anion-exchange resins is not very great, and with few exceptions their standard is lower than in the corresponding field of research on cation-exchange resins[1].

The lag in studies on the thermal stability of anion-exchange resins is due to the inadequate systematic approach to the problem, the competitive reactions which frequently occur simultaneously, and to a certain extent the smaller availability of the specimens for study than in the case of cation-exchange resins.

Systematic studies on the thermal stability of anion-exchange resins began only after the development of reliable methods for the separate determination of their exchange capacities with respect to active groups of different basicity. Further development of studies in this field depends largely on the validity of the methods employed by investigators.

As in the original reports, attention is concentrated on AV-17 anion-exchange resin and its analogues which have been most widely used under industrial conditions.

II. METHODS FOR INVESTIGATING THE THERMAL STABILITY OF ANION-EXCHANGE RESINS

This section deals with methods which are of specific importance for anion-exchange resins. Technical anion-exchange resins are first freed from impurities by prolonged treatment in a column or on a filter with 3 N hydrochloric acid and then washed with water and converted into the hydroxide-form by passage of 1 N aqueous KOH solution. To condition the resins, the above operations are repeated twice and the last washing with water is terminated as soon as the consumption of 0.01 N hydrochloric acid in the titration of 100 ml of wash liquid falls to 0.3 ml.

When necessary, the anion exchanger is converted into a salt-form by passing through the column a 0.5 N solution of the corresponding acid until its concentration in the filtrate remains constant. To avoid hydrolytic scission of counterions, weakly basic anion exchangers are washed free of the electrolyte with 96% ethanol until the filtrate gives a neutral response.

Anion-exchange resins are heat-treated in air in weighing bottles or in other vessels suitable for weighing[5] and, when an aqueous or organic medium is employed, the heat treatment is in an open or sealed tube[10]. The devices recommended by the authors of this review[11] are very convenient for the investigation of gaseous nitrogen-containing compounds formed on heat treatment of anion-exchange resins.

After the specified duration of heat treatment has elapsed, the anion exchanger is repeatedly washed with deionised water until a neutral response is obtained with respect to phenolphthalein and the phases are investigated separately.

In the simplest case, the total content of basic substances is determined in the liquid phase (called the aqueous extract) by titration with hydrochloric acid [5]. In more complex cases, the substances passing to the aqueous extract and representing the resin degradation products are identified by general chemical [3,12,13], potentiometric [12], and spectrophotometric [12] methods. Finally, many investigators [14-17] disregard the aqueous extract, confining themselves to a more or less detailed study of the anion exchangers themselves before and after their thermochemical [14-16] or radiation [17] treatment. In the study of the mechanism of the changes occurring in anion-exchange resins, as in the determination of small losses of exchange capacity which are not revealed by the direct investigation of the solid phase, such limitation of the research technique used is completely unjustified.

An example of the most complete investigation of an ion-exchange resin after thermochemical treatment is that of Vinogradov and Kazantsev [14]. The authors determined the exchange capacity of the anion-exchange resin with respect to strongly and weakly basic groups, the total nitrogen content, and the physicochemical characteristics of the resin, such as absorption in the infrared spectrum, density, and the coefficieint of the moisture absorption capacity. Among the above properties, all the investigators attribute the greatest importance to the exchange capacity, for the determination of which a wide variety of methods have been developed, but these require a rigorous and critical approach.

A compilation of methods for the determination of the exchange capacity of anion-exchange resins and the relevant recipes may be found in monographs [18-20] and in an All-Union Standard [21]. All the methods for the determination of the static exchange capacity (SEC) taking into account without discrimination a proportion of the active groups which depends on the specific conditions of the analysis should be ignored. We believe that best results in the study of the thermal stability of anion-exchange resins can be obtained by the following method for the determination of the exchange capacity.

A differential determination of the strongly and weakly basic groups is provided for in Kunin's method [22], which was perfected in studies by English [23,24] and Czech [25] investigators. According to the evidence of Polak and Wyroba [26], Kunin's original method gives somewhat high values for the content of weakly basic groups. More reliable results were obtained using Stamberg's version [25]. With certain additional modifications, the method has been used to determine the exchange capacities of anion-exchange resins mixed with cation-exchange resins [27].

A direct determination of groups with different basicities without a preliminary conversion of the anion-exchange resins into a salt-form is achieved in the method of Polyanskii and Shaburov [28].

Studies of Kopylova and coworkers [29,30] on the use of non-aqueous media for the separate determination of primary, secondary, and tertiary amino-groups in anion-exchange resins are of great practical importance.

The methods of Fischer and Kunin [22] and Polyanskii et al. [31] yield the best results in the determination of the exchange capacities of anion-exchange resins in the Cl-form. In the method of Fischer and Kunin [22], it is recommended that the resin be washed in a column with 4% aqueous K_2SO_4 solution with subsequent titration of chloride ions in the filtrate by Mohr's method. Polyanskii and Shaburov [31] proposed a simpler static version of the method based on the titration of the Cl^- ions evolved on interaction of the anion-exchange resin with 10% aqueous K_2SO_4 solution without the separation of the phases.

Since strongly and weakly basic groups present in polyfunctional anion-exchange resins exhibit different thermal stabilities, the state of the anion-exchange resin can be fully characterised only by the separate determination of these groups; the method of expressing their concentrations is then important.

The majority of investigators assess the thermal stabilities of anion-exchange resins on the basis of the time variation of the exchange capacity or from the relative loss of exchange capacity R:

$$R = \frac{E_0 - E_t}{E_0} \cdot 100\% \ , \qquad (1)$$

where E_t and E_0 are the exchange capacities after and before this treatment. It is noteworthy that these criteria, in particular for polyfunctional anion-exchange resins, are only of relative value, since for a first-order reaction R is independent of the initial exchange capacity [32]. In studies on thermal stability, the exchange capacity of anion-exchange resins is referred to 1 g of dry (E^d) or swollen (E^h) resin and sometimes is expressed in fractions of the conversion of the functional groups [33,34]. One should note that all these quantities depend on many variables (the amount of bound water, the weight of functional groups, the type of counterions) and therefore they are unsuitable for the kinetic treatment of the experimental data when the ion-exchange resins are heated or irradiated.

As a rule, the most stable component of the resin is the matrix. Therefore in kinetic studies the exchange capacity is referred to 1 g of the matrix (E^M) without functional groups, counterions, and sorbed water.

The wide variety of existing methods for expressing the exchange capacities of ion-exchange resins hinder the comparison of the experimental data obtained by different investigators and require the derivation of conversion formulae in each case. Such recalculations are facilitated by the relations presented in Table 1 and in Eqns. (2)–(6), which are valid for all types of ion-exchange materials.

Table 1 may be supplemented by formulae for the calculation of exchange capacity when the ionic form changes from B to A, which can be written as follows for the dry and swollen resins [32]:

$$E_A^d = \frac{E_B^d}{1 + E_B^d(\epsilon_A - \epsilon_B)} \ , \qquad (2)$$

$$E_A^h = \frac{(1 + K_B)E_B^h}{(1 + K_A)[1 + E_B^h(1 + K_B)(\epsilon_A - \epsilon_B)]} \ . \qquad (3)$$

In the corresponding change of the ionic form of only one type (i) of functional groups in a polyfunctional resin [32], we have

$$E_{i,A}^d = \frac{E_{i,B}^d}{1 + E_{i,B}^d(\epsilon_{i,A} - \epsilon_{i,B})} \ , \qquad (4)$$

$$E_{i,A}^h = \frac{(1 + K_B)E_{i,B}^h}{(1 + K_{i,A})[(1 + K_B)E_{i,B}^h(\epsilon_{i,A} - \epsilon_{i,B}) + 1]} \ , \qquad (5)$$

where K is the coefficient of moisture absorption capacity in g H_2O/g dry resin, E the exchange capacity in mequiv. g^{-1}, ϵ the equivalent weight of the functional groups with counterions A or B, $K_{i,A}$ the coefficient of

Table 1. Formulae for the recalculation of the exchange capacities of ion-exchange resins.

Resin exchange capacity	E^h	E^d	E^M	N^h	N^d	N_c^h	N_c^d
$E^h = \frac{\text{mequiv.}}{\text{g swollen resin}}$	E^h	$\frac{E^d}{1+K}$	$\frac{E^M}{(1+\sum_{i=1}^{n} E_i^M \epsilon_i)(1+K)}$	$\frac{N^h}{d^h}$	$\frac{N^d}{(1+K)d^d}$	$\frac{N_c^h}{d^h\epsilon^h}$	$\frac{N_c}{(1+K)\epsilon^d d^d}$
$E^d = \frac{\text{mequiv.}}{\text{g dry resin}}$	$E^h(1+K)$	E^d	$\frac{E^M}{1+\sum_{i=1}^{n} E_i^M \epsilon_i}$	$\frac{N^h(1+K)}{d^h}$	$\frac{N^d}{d^d}$	$\frac{N_c^h(1+K)}{d^h\epsilon^h}$	$\frac{N_c^d}{\epsilon^d d^d}$
$E^M = \frac{\text{mequiv.}}{\text{g resin matrix}}$	$\frac{E^h}{\frac{1}{1+K}-\sum_{i=1}^{n} E_i^h \epsilon_i}$	$\frac{E^d}{1-\sum_{i=1}^{n} E_i^d \epsilon_i}$	E^M	$\frac{N^h}{\frac{d^h}{1+K}-\sum_{i=1}^{n} N_i^h \epsilon_c}$	$\frac{N^d}{d^d-\sum_{i=1}^{n} N_i^d \epsilon_i}$	$\frac{N_c^h}{\frac{d^h\epsilon^h}{1+K}-\sum_{i=1}^{n} N_{ki}^h \epsilon_i}$	$\frac{N_c^d}{d^d\epsilon^d-\sum_{i=1}^{n} \Sigma_{ki}^d \epsilon_i}$
$N^h = \frac{\text{mequiv.}}{\text{ml swollen resin}}$	$E^h d^h$	$\frac{E^d d^h}{1+K}$	$\frac{E^M d^h}{(1+K)(1+\sum_{i=1}^{n} E_i^M \epsilon_i}$	N^h	$\frac{N^d d^h}{(1+K)d}$	$\frac{N_c^h}{\epsilon^h}$	$\frac{N_c^d d^h}{(1+K)\epsilon^d d^d}$
$N^d = \frac{\text{mequiv.}}{\text{ml dry resin}}$	$E^h(1+L)d^d$	$E^d d^d$	$\frac{E^M d^d}{1+\sum_{i=1}^{n} E_i^M \epsilon_i}$	$\frac{N^h(1+K)d^d}{d^h}$	N^d	$\frac{N_c^h(1+K)d^d}{\epsilon^h d^h}$	$\frac{N_c^d}{\epsilon^d}$
$N_c^h = \frac{\text{mequiv.}}{\text{ml swollen resin in column}}$	$E^h d^h \epsilon^h$	$\frac{E^d d^h \epsilon^h}{1+K}$	$\frac{E^M d^h \epsilon^h}{(1+K)(1+\sum_{i=1}^{n} E_i^M \epsilon_i)}$	$N^h\epsilon^h$	$\frac{N^d d^h \epsilon^h}{(1+K)d^d}$	N^h	$\frac{N_c^d d^h \epsilon^h}{(1+K)d^d\epsilon^d}$
$N_c^d = \frac{\text{mequiv.}}{\text{ml dry resin in column}}$	$E^h(1+K)\epsilon^d d^d$	$E^d d^d \epsilon^d$	$\frac{E^M d^d \epsilon^d}{1+\sum_{i=1}^{n} E_i^M \epsilon_i}$	$\frac{N^h(1+K)\epsilon^d d^d}{d^h}$	$N^d\epsilon^d$	$\frac{N_c^h(1+K)\epsilon^d d^d}{E^h d^h}$	N_c^d

moisture absorption capacity of the resin in which the groups i are in the A-form and the rest are in the B-form, and d is the density of the resin in g ml^{-1}.

When the ionic forms of all the functional groups change the exchange capacity with respect to one of them designated as the first is given by the following formula for the simplest case of the coexistence of two different functional groups [32]:

$$E_{1,A}^d = \frac{E_{1,B}^d(1+E_2^M \cdot \epsilon_{2,B})}{1+E_2^M \cdot \epsilon_{2,A}+E_{1,B}^d(\epsilon_{1,A}-\epsilon_{1,B})+E_{1,B}^d \cdot E_2^M(\epsilon_{1,A} \cdot \epsilon_{2,B}-\epsilon_{1,B} \cdot \epsilon_{2A})} \cdot \quad (6)$$

where the subscripts $1,A$ and $2,B$ imply that the capacity or the equivalent weight refers to the first type of functional groups in the ionic form A or to the second type of groups in the ionic form B.

In order to be able to employ the above formulae, it is necessary to know the densities d of the dry and swollen resins, the coefficient of moisture absorption capacity, and the degree of filling of the columns ϵ. The derivation of these quantities was considered in the preceding review [1]. However, in the measurement of the coefficient of moisture absorption capacity for strongly basic anion-exchange resins in the OH-form, one cannot employ the trivial method, since in the dehydration stage not only water but also nitrogen-containing compounds volatilise [5].

A compromise solution was proposed by Greben' [32], who employed the relatively high thermal stability of the salt-forms of ion-exchange resins. He derived a formula for the calculation of the coefficient of moisture absorption capacity K_A of the ionic forms A which decompose on drying, in terms of the weight of the swollen resin p in forms A and B, the corresponding equivalent weights of the functional groups, the exchange capacity, and the coefficient of moisture absorption capacity K_B of the thermostable form B:

$$K_A = \frac{(1+K_B)\,p_{A/p_B}^h}{1-(1+K_B)E_B^h(\epsilon_B-\epsilon_A)} - 1 \cdot \quad (7)$$

A decrease in the content of the functional groups is accompanied by a decrease in the weight of the resin, which is given by the following formula in the absence of degradation of the matrix to soluble oligomers:

$$W_{exp} = \frac{p_0^d - p_t^d}{p_0^d} \cdot 100\,\% = \left[1 - \frac{p_t^h(1+K_0)}{p_0^h(1+K_t)}\right] \cdot 100\,\% \cdot \quad (8)$$

The experimental weight losses can be usefully compared with the calculated values W_{calc}, which are given by the following expression when the condition mentioned above is fulfilled:

$$W_{calc} = (1+K_0)\sum_{i=1}^{n}\left(E_{0,i}^h - E_{t,i}^h \frac{p_t^h}{p_0^h}\right)\epsilon_i \cdot 100\,\% =$$

$$= \sum_{i=1}^{n}\left(E_{0,i}^d - E_{t,i}^d \frac{p_t^d}{p_0^d}\right)\epsilon_i \cdot 100\,\% = \frac{\sum_{i=1}^{n}(E_{0,i}^M - E_{t,i}^M)\,\epsilon_i}{1+\sum_{i=1}^{n} E_{0,i}^M \epsilon_i} \cdot 100\,\% \cdot \quad (9)$$

The satisfactory agreement between W_{exp} and W_{calc}, established in a study of the thermal stability of AV-17 anion-exchange resin [35] demonstrates the absence of degradation of the matrix to soluble oligomers under the experimental conditions.

To characterise the processes involved in the loosening or contraction of the three-dimensional network but not the breakdown of the matrix, it is useful to employ the equivalent coefficient of moisture absorption capacity K^e:

$$K^e = \frac{K}{0{,}018\,E^d} = \frac{K}{0{,}018\,(1+K)\,E^h} \cdot \quad (10)$$

Eqn. (10) shows that the equivalent coefficient of moisture absorption capacity defines a number of millimoles of water per milliequivalent of functional groups provided the entire trapped liquid is in a bound state and does not merely fill pores, cracks, etc. and that the hydration shells of adjacent groups do not overlap [36,37].

In certain cases, the formation of cracks leads to an increase of the equivalent coefficient of moisture absorption capacity[37], which is in no way related to the expansion of the three-dimensional network. The decrease of this quantity for the usual gel cation-exchange resins may indicate a contraction of the three-dimensional network while for macroporous resins it may be evidence of a decrease of the overall porosity. In the literature on ion exchange, publications have already appeared in which the effect of heat treatment on the porometric characteristics of cation-exchange resins is considered[38,39]. Similar studies have not so far been made on anion-exchange resins.

Infrared spectroscopic methods are particularly important for the investigation of the changes in the chemical structure of anion-exchange resins on heat treatment and irradiation. The basic aspects of the application of infrared spectroscopy to anion-exchange resins have already been considered[14,140]; in addition, interesting experimental results have been presented in other publications[41-44].

In many cases, comparison of the results of different workers is difficult owing to the absence in the reports of a detailed description of the resins investigated (the degree of their cross-linking, capacity with respect to different active groups, and the coefficient of moisture absorption capacity) and sometimes due to an unduly concise description of the experimental technique. For example, such details as the proportions of the resin and solution phases are undeservedly regarded as unimportant and are usually not mentioned. Nevertheless, in cases where there is a direct interaction of the medium with the functional groups[44], when the products of the reaction affect its rate[27], and for reversible changes in resins, the kinetics of the decrease of exchange capacity depend on the quantitative proportions of the phases. Naturally, there are no grounds for being dogmatic about these relations, but it is important that each investigator base his treatment on something concrete.

III. THE STABILITY OF ANION-EXCHANGE RESINS ON HEATING IN AIR

The study of the thermal stability of anion-exchange resins in air was begun in 1952 [45] and was confined to the observation of an endothermic effect associated with the evolution of water and an exothermic effect associated with the combustion of the resin. In another, more sophisticated study[46], the thermal stability of an anion-exchange resin based on methylvinylpyridine and divinylbenzene was investigated but in this case the change in the content of acid groups was not determined by chemical analysis.

Two endothermic effects observed on the thermogram for AV-17 anion-exchange resin in the OH-form have been interpreted[47]: the first (at 120–150°C) was attributed to the desorption of water and the elimination of active groups and the second (at 190–280°C), to the thermal degradation of the resin itself. Together with the decrease of exchange capacity, heat treatment results in a decreased capacity of the anion-exchanger for hydration, but it is not surprising that below 140°C these effects are not observed.

Comparative thermographic data for the stability of anion-exchange resins of different basicities have been published[48,49]. In studies on EDE-10P, Dowex-1 × 4 and Dowex-2 × 4 resins, differences between the stabilities of strongly and weakly basic active groups have been clearly demonstrated: a decrease of exchange capacity is observed mainly in relation to strongly basic groups. EDE-10P anion-exchange resin in the OH-form is stable in air up to 150°C, but in the range 160–200°C strongly basic groups are converted into weakly basic groups without loss of the total exchange capacity[48]. Strongly basic polymerisation anion-exchange resins lose thier active groups completely after heating for 3 h at 220°C.[49]

As shown by one of the present authors and Shaburov[5], even simple drying of AV-17 anion-exchange resin at room temperature entails an appreciable decrease of the total exchange capacity with a simultaneous accumulation of weakly basic groups. Following Dybczynski[50], the authors explained these changes by deamination:

$$R{-}CH_2{-}N(CH_3)_3OH + H_2O \rightarrow R{-}CH_2OH + NH(CH_3)_3OH \qquad (11)$$

and degradation

$$R{-}CH_2{-}N(CH_3)_3OH + H_2O \rightarrow R{-}CH_2{-}NH(CH_3)_2OH + CH_3OH\ . \qquad (12)$$

However, one cannot rule out the possibility that reactions (11) and (12) are of subsidiary importance and that the main cause of the changes in the capacity of AV-17 anion-exchange resin is interaction of two active groups with formation of a tetramethylammonium base and of two polymeric molecules, one of which should be a weakly basic anion exchanger:

$$\begin{matrix} R{-}CH_2{-}N(CH_3)_3OH \\ R{-}CH_2{-}N(CH_3)_3OH \end{matrix} + H_2O \rightarrow \begin{matrix} R{-}CH_2{-}NH(CH_3)_2OH \\ R{-}CH_2OH \end{matrix} + N(CH_3)_4OH\ . \qquad (13)$$

Mechanism (13) is supported primarily by the fairly high basicity of the aqueous extracts from AV-17 anion-exchange resin dried *in vacuo*, which may be attributed to the tetramethylammonium base the volatility of which is known[51] to be low in aqueous solutions. Furthermore, mechanism (13) is confirmed by the finding that the rates of deamination and degradation of anion-exchange resins depend little on the method of drying[5].

Thus AV-17 × 2 anion-exchange resins dried at room temperature *in vacuo*, at room temperature in the presence of $CaCl_2$ and Anhydrone, and at 110°C to constant weight lost 1.69, 1.57, and 1.96 milliequivalents of strongly basic groups per gramme of dry resin as a result of deamination and 1.42, 1.15, and 1.89 mequiv. g^{-1} as a result of degradation. Under the same drying conditions, AV-17 × 16 resin lost 0.44, 0.37, and 0.68 mequiv. g^{-1} as a result of deamination and 0.39, 0.39, and 0.56 mequiv. g^{-1} as a result of degradation. All these findings make it possible to regard the deamination and degradation of the OH-form of AV-17 anion-exchange resin as coupled and not as independent processes.

Bearing in mind the comparatively low volatility of the conversion product of AV-17 anion-exchange resin according to mechanism (13), it is easy to explain the finding of Soldatov et al.[52] that its exchange capacity remains unchanged when dried at 60°C. Indeed, this constancy is only an apparent consequence of the equivalent relations between the number of strongly basic groups eliminated and the tetramethylammonium base formed and remaining in the resin phase under mild drying conditions. If the analysis of liquid extracts is neglected it is thus possible to arrive at completely incorrect ideas about the stability of the anion-exchange resin.

In AV-27 anion-exchange resins, the ethanol group is linked to the nitrogen atom less strongly than the methyl groups[13] and therefore the main cause of the changes in the

resin is degradation with elimination of ethylene glycol according to the equation

$$\begin{matrix}RCH_2N(CH_3)_2OH\\ |\\ CH_2CH_2OH\end{matrix} + H_2O \rightarrow \begin{matrix}RCH_2N(CH_3)_2OH\\ |\\ H\end{matrix} + HO{-}CH_2CH_2{-}OH \ . \quad (14)$$

Shaburov and Saldadze's studies[53] on the behaviour of the polyfunctional AV-16 anion-exchange resin in the OH-form involving a large scale employment of chemical-analytical methods showed that at 110°C the capacity decreases mainly in relation to the strongly basic pyridinium groups, which the authors believe to undergo tautomeric transformations. The changes in exchange capacity during the drying process lead to a marked contraction of the three-dimensional network and to a decrease of swellability almost by a factor of two.

The salt-forms of AV-17 anion-exchange resin[44,49,54-56] and of anion exchangers based on polyallylamine and epoxide ethers[57] are in general more resistant to heat treatment in air than the corresponding resins in the hydroxide-form. The salt-forms derived from acids with non-oxidisable anions can be arranged in the following sequence in terms of the decrease of thermal stability: $RCl > R_2SO_4 > R_3BO_3$. The relative thermal stability of the nitrate-form depends on temperature[49,58]. At 140°C it is more resistant to heating than the hydroxide-form, while at 160–200°C it undergoes pyrolytic decomposition and self-ignition. The self-inflammation temperature decreases with increased degree of cross-linking of Dowex-1 anion-exchange resin and with the concentration of the nitric acid employed for its regeneration. Barghusen and Jonke[58] do not recommend the employment of the nitrate-form of the resin above 60°C and note that, other conditions being equal, the thermal stability of anion-exchange resins in this form decreases in the series Dowex 2 > Permutit SK > Amberlite IRA-401.

Anion-exchange resins of type AV-17 in the Cl-form are entirely stable on heating in air up to 70°C [55] and, according to Shaburov[54], up to 100°C; they even withstand brief heating at 160°C.[35]

On prolonged heating at a temperature as low as 130°C, active groups of different basicities are split off, tentatively[55] in accordance with the mechanisms

$$RCH_2N(CH_3)_3Cl \rightarrow RCH_2Cl + N(CH_3)_3 \ , \quad (15)$$

$$RCH_2NH(CH_3)_2Cl \rightarrow RCH_2Cl + HN(CH_3)_2 \ . \quad (16)$$

A further increase of temperature from 130° to 180°C leads to a sharp fall of exchange capacity in relation to strongly basic groups with a possible accumulation of weakly basic groups owing to degradation:

$$RCH_2N(CH_3)_3Cl \rightarrow RCH_2N(CH_3)_2 + CH_3Cl \ . \quad (17)$$

It has been shown[35,44] that the number of weakly basic groups formed on heating AV-17 resin in a mixed Cl–OH-form to 150–170°C is smaller by a factor of two than the number of strongly basic groups split off under these conditions and it has been established that the scission of these groups is not due to the reactions (15)–(17) but is a result of hydrolysis involving the residual water. In the presence of a high water content, one amino-group is involved in the hydrolysis:

$$RCH_2N(CH_3)_3Cl + H_2O \rightarrow RCH_2OH + HN(CH_3)_3Cl \ , \quad (18)$$

and in the presence of a deficiency of water two amino-groups are involved:

$$\begin{matrix}RCH_2N(CH_3)_3Cl\\ RCH_2N(CH_3)_3Cl\end{matrix} + H_2O \rightarrow \begin{matrix}RCH_2OH\\ RCH_2NH(CH_3)_2Cl\end{matrix} + N(CH_3)_4Cl \ . \quad (19)$$

If the anion-exchange resin is dried *in vacuo* at 100°C, reaction (18) altogether fails to take place owing to the insufficiency of water and hydrolysis via mechanism (19) probably involves the interaction of two amino-groups via the following mechanism:

$$\begin{matrix}RCH_2N(CH_3)_3Cl\\ RCH_2N(CH_3)_3Cl\end{matrix} \rightarrow \begin{matrix}RCH_2\\ RCH_2\end{matrix}\!\!>\!N(CH_3)_2Cl + N(CH_3)_4Cl \ . \quad (20)$$

When AV-17 anion-exchange resins in the Cl-form are heated in open tubes to 150–180°C, partial decomposition of tetramethylammonium chloride is possible[44]. An increase of temperature to 270°C leads to the total loss of exchange capacity and to the appearance of inactive nitrogen[55], possibly owing to the oxidation of the amino-groups by atmospheric oxygen to nitro-groups.

EDE-10P anion-exchange resin in the Cl-form is less resistant to heating than in the mixed Cl–OH-form[35], since the HCl evolved in the hydrolysis of the weakly basic groups decomposes the anion-exchanger macromolecule. Condensation anion-exchange resins of type AT are more stable than EDE-10P resin[57], the increase of stability in the series AT-7 < AT-8 < AT-6 being explained (without convincing evidence) by different relative contents of primary, secondary, and tertiary amino-groups. The above anion exchangers were investigated by the thermographic method[57], which showed the presence of an endothermic effect in the range 160–200°C corresponding to the degradation of the functional groups. The differential thermal (DTA) curves for a number of strongly basic anion exchangers in salt-forms are quoted in a number of publications[48,49,52].

The resistance of anion-exchange resins in salt- and hydroxide-forms to frost has been investigated[59,60] and it has been established that the main result of the action of low temperatures is disruption of some of the polymeric chains, the cracking of grains, and deamination; degradation was not observed[59].

The thermal stability of anion-exchange resins with phosphonium and sulphonium groups[61] is appreciably lower than that of quaternary ammonium bases with an analogous matrix structure.

IV. THERMAL STABILITY OF ANION-EXCHANGE RESINS IN WATER AND AQUEOUS SOLUTIONS

Isolated data for the thermal stabilities of anion-exchange resins in water were obtained incidentally by the authors of the first studies of the properties[62,63] and behaviour of anion-exchange resins under the conditions of their industrial employment[64-68]. A general characteristic of these investigations is the random choice of the objects of study, the inadequate reliability of the experimental methods employed, and the formal nature of the results, which do not always yield a consistent picture of the main phenomenon during heat treatment—the decrease of the exchange capacity of the anion-exchange resin.

Systematic studies on the thermal stability of a wide range of different types of anion-exchange resins were undertaken by Pashkov et al.[3] On the basis of extensive experimental data, the authors showed that the thermal stability of anion-exchange resins depends on the matrix structure and on the nature of the active groups and the counterion. Thus weakly basic resins proved to be more stable than strongly basic resins and their salt-forms proved to be more stable than the hydroxide-forms. Other conditions being equal, polymerisation anion-exchange resins are more stable than condensation resins, although

individual examples of the latter, for instance EDE-10P resin [3] and particularly AT-6 resin [69], exhibit a high stability. Unfortunately all the experiments were carried out by Pashkov et al. [3] only at a single temperature (100°C) and for a single duration of heating (60 h) and the chosen criterion of thermal stability was the static exchange capacity, which is known [70] to depend on the conditions of its determination.

Table 2. Thermal stabilities of a series of anion-exchange resins in the OH-form

Type of anion-exchange resin	Active groups	Temp., °C	Time, h	Relative change in exchange capacity, %			References
				total	w.r.t. strongly basic groups	w.r.t. weakly basic groups	
AV-17	$-\overset{+}{N}(CH_3)_3$	100	48	+33	+18	+60	73
		100	120	+36	+29	+48	73
		100	120	+12	+19	−6	74,75
		100	240	+33	+35	+29	73
		100	240	+16	+23	−5	75
AV-27	$-\overset{+}{N}(CH_3)-CH_2-CH_2OH$	100	48	+17	+52	−54	73
		100	120	+28	+63	−44	73
		100	120	+13	+80	−63	75
		100	240	+18	+87	−67	75
		120	48	+36	+93	−81	73
		120	120	+44	+95	−59	73
AN-22	$-NH_2$, >NH	120	120	+2	—	—	73
AV-16	>N, >NH,	150	120	+26	+86	—	75
	$\overset{+}{N}$–	150	240	+27	+86	—	75
EDE-10P	>N, >NH, $\overset{+}{N}$<	150	48	+10	+71	2	73
		150	120	+11	+75	2	73
AN-2F	N<	150	24	—	—	90	71

Additional information about the thermal stability of various anion-exchange resins in the OH-form can be found for a wider temperature range in studies by Ol'shanova and coworkers [71-73]. The most important results obtained in the above investigations are presented in Table 2, where the plus sign before the value of the relative change in exchange capacity of the anion-exchange resin as a result of its heat treatment corresponds to a decrease and the minus sign to an increase of exchange capacity.

Comparison of the results in Table 2 reveals primarily a poor agreement between the values of exchange capacity losses established by different workers. This is most probably due to the non-equivalence of the resins investigated, which might have differed in the degree of cross-linking and in the composition of the samples used. For example, 6% of the exchange capacity corresponded to the contribution by the weakly basic groups of AV-17 resins in the study by Shaburov et al. [74], while in the study by Petrova and Potakova [73] the corresponding percentage was **36.** The divinylbenzene content of the AV-17 anion-exchange resins has been indicated only by Shaburov et al. [74] and is not mentioned in the other investigations. This significant omission vitiates the experimental results no less than the use of faulty research techniques.

Bearing in mind the above inconsistency, it is necessary to compare the results of the determination of the losses of capacity obtained in the same laboratory. In this connection, the data in Table 2 lead to the conclusion that the stabilities of polymerisation and condensation anion-exchange resins with weakly basic groups are different. For anion-exchange resins with strongly basic groups, these differences become blurred, since, owing to the $-I$-effect in quaternary ammonium bases [76], the linkage with $C-\overset{+}{N}$ is so highly polarised that the structure of the framework becomes of secondary importance as a factor in thermal stability. Moreover, this levelling is favoured by the poor choice by the authors of the above studies of the relative change in capacity as a criterion of the thermal stability of anion-exchange resins known to have different contents of active groups.

The decrease of the exchange capacity of anion-exchange resins in the OH-form in relation to strongly basic groups has been shown [10,12,13,77] to take place owing to the deamination and degradation processes examined above, which are usually identified with the familiar Hofmann degradation [78]. The methanol and trimethylamine formed on heat treatment of AV-17 anion-exchange resins were identified; according to Shaburov and Saldadze [12] and Roginskaya et al. [77], their amounts corresponded to changes in exchange capacity with respect to strongly and weakly basic groups. However, the data in Roginskaya's disseration [79] and in the study of Minto et al. [112] contradict this assertion.

The relative contribution by the deamination and degradation of AV-17 anion-exchange resins depends on the duration of heat treatment and on the content of divinylbenzene (DVB) in the test object [74]. In the first, rapid stage involving the decrease of exchange capacity, the ratio of the rates of these reactions changes with increase of the degree of cross-linking in favour of deamination, which has been explained [74] by a weakening of the protective effect of the hydration shells of the active groups as the swellability of the resin decreases. Generalising such data [71,72,80,84,112], we may note that in the majority of cases an increase of the content of the cross-linking agent entails a decrease of the thermal stability of strongly basic anion exchangers in the OH-form.

Not only the variation of the degree of cross-linking but also an increase in the specified purity of the starting material employed in the synthesis and the introduction of active groups into mixed aliphatic-aromatic [81] or even aliphatic [82] structures give rise to some possibility of controlling the thermal stability. For example, it has been established that [80] the anion-exchange resin based on styrene and *p*-divinylbenzene has a higher resistance to heating than the specimen synthesised from technical DVB, the impurities of which cause the formation of defects in the macromolecule. An improved thermal stability of strongly basic anion-exchange resins in which the active group is separated from the aromatic ring by the isobutyl group has been predicted [81].

AV-27 anion-exchange resin, which occupies an intermediate position as regards thermal stability, and its analogue Amberlite IRA-410, readily split off the CH_2CH_2OH group with formation of ethylene glycol and a high-molecular-weight tertiary amine (degradation) [13]. This process is faster than the overall deamination and degradation of AV-17 resin and is responsible for the higher rate of decrease of the exchange capacity of AV-27 resin in relation to strongly basic groups.

An interesting study on the thermal stability of the vinylpyridine anion-exchange resin VP-IAP in water and certain aqueous solutions has recently been made by Kiseleva et al.[43] On the basis of a large-scale experiment by the infrared spectroscopic method, they showed that heating the anion-exchanger in water at 200–230°C for 10–60 h leads not only to the usual losses of exchange capacity but also to the oxidation of the methyl groups of the ring to aldehyde and carboxy-groups and to the formation of hydroxypyridines. In alkaline solutions, the formation of a stable form of pyridones accompanied by the loss of exchange capacity is observed. If the heat treatment of the anion exchanger was carried out at 70°C, the pyridones formed were protonated to hydroxypyridines with restoration of exchange capacity on subsequent heating of the anion exchanger in water or nitric acid solutions at 200°C.

The resistance of strongly basic anion-exchange resins and model low-molecular-weight quaternary ammonium bases to heating in alkaline media has been investigated[82-87] and it has been established that resins of the phenyl type, like the corresponding low-molecular-weight bases with aromatic substituents, undergo mainly deamination (to the extent of 60–70%). Anion exchangers of the benzyl type and quaternary ammonium bases with benzyl substituents largely undergo the Hofmann degradation, its rate being higher than for aliphatic alkyltrimethylammonium bases[82]. Hence it follows that the synthesis of anion-exchange resins with aliphatic structures constitutes a likely pathway to the creation of thermostable polyme. with anion-exchange properties.

In a later study[87], it was shown that at 40–100°C macroporous ion-exchange resins are more stable in 2–10 *N* solutions of alkali than gel ion exchangers; similar observations were made in studies on the thermal stability of macroporous sulphonic acid cation-exchange resins[39]. Studies in this field should be continued and require theoretical consideration.

Data for the stability of anion exchangers in solutions of alkalis and non-oxidising acids, which are of interest for practical purposes, have been published[15,87,89]. The studies of Laskorin et al.[15] led to the establishment of a norm for the prolonged employment of a number of USSR-produced anion-exchange resins, which are listed in Table 3.

All the inorganic reagents investigated can be arranged in the following sequence in terms of their influence on the rate of decrease of the exchange capacity of anion-exchange resins: $NaOH > NH_4OH > Na_2CO_3 > HNO_3 > H_2SO_4$. Thus the disrupting capacity of alkalis is greater than that of acids (even the oxidising nitric acid). In nitric acid solutions at a concentration up to 6 *N*, AM and AMP anion-exchange resins can be used only at room temperature, while VP-IA resin can be used up to 80°C. According to other data, the exchange capacity of the anion-exchange resins AN-23, AN-25, AN-27, AN-35, AN-40, and AN-42 based on vinylpyridine is hardly altered after heating for 90 h in 5 *N* HNO_3 at 100°C.[88]

The salt-forms of strongly basic anion-exchange resins are more stable than the hydroxide-forms not only on heating in an aqueous medium[3,54,71,90,91] but also on treatment with corrosive agents such as free chlorine[62].

In hydrogen peroxide solutions at concentrations up to 1 M, the stability of AM-6, AMP, and VP-IA anion-exchange resins decreases in the order in which they have been stated. The addition of 0.2 *N* KOH to hydrogen peroxide enhances its oxidising activity and the addition of 0.2 *N* H_2SO_4 reduces it. The anion-exchange resins exhibit a particularly low stability in calcium hypochlorite solutions.

Disdar[92] and Bychkov et al.[93] made the most interesting and complete investigation of the behaviour of AV-17 anion-exchange resins in hydrogen peroxide solutions. It was shown[93] that AV-17 anion-exchange resins absorb selectively hydrogen peroxide as a result of the displacement of water and the exchange sorption of the HO_2^- ion. Hydrogen peroxide then undergoes catalytic decomposition and the anion exchanger undergoes deamination and degradation; the catalytic activity of the anion exchanger in the decomposition of hydrogen peroxide decreases faster than the exchange capacity in relation to strongly basic groups. An increase of the concentration of the oxidant leads to an increase of the loss of exchange capacity by the anion exchanger and an increase of the amount of carbon dioxide given off. Owing to their partial oxidation, the amount of amines determined is somewhat lower than the value calculated from the loss of the exchange capacity of the resin. Strongly basic anion-exchange resins in the Cl-form and weakly basic anion exchangers in the OH-form decompose to a lesser extent[93].

Table 3. The limiting permissible operational standards for anion-exchange resins in solutions of acids and alkalis.

Reagent	Standards for stable operation of anion-exchange resins					
	AM		AMP		VP-IA	
	normality of reagent	temp., °C	normality of reagent	temp., °C	normality of reagent	temp., °C
H_2SO_4	0.1—17	20—80	0.1—17	20—80	0.1—17	20—80
HNO_3	up to 6	not more than 20	up to 6	not more than 20	0.1—6	20—80
HNO_3	less than 1	20—80	less than 1	up to 80		
NaOH	0.1—3	20—80	less than 0.01	20	0.1	not more than 20
NH_4OH	—	—	less than 0.1	up to 20	up to 3	20—80
Na_2CO_3	—	—	up to 3	30	up to 3	50

Vinogradov's dissertation[94] has made a significant contribution to the elucidation of the mechanism of the action of oxidants on anion-exchange resins. He showed that the ionogenic groups are involved in reactions of three types: deamination, degradation, and inactivation. Oxidants mainly induce inactivation, i.e. the loss of the capacity of the functional groups to participate in ion exchange. Moreover, oxidants act on the matrix, causing the formation of new functional groups containing a C=O double bond. With increase of the divinylbenzene content in the anion-exchange resin, the number of these groups also increases; there is a simultaneous intensification of degradation and a decrease of the contribution by deamination. Anion-exchange resins containing pyridine or quinoline groups are the most resistant to the action of oxygen. In all the oxidants investigated, except solutions of ammonium persulphate, they withstand heating to 80°C. Weakly basic anion-exchange resins in oxidant solutions are less stable than strongly basic resins, although in pure water the opposite behaviour was observed. The change in the composition of the medium probably alters the mechanism of the processes occurring.

V. THERMAL STABILITY OF ANION-EXCHANGE RESINS IN ORGANIC AND MIXED MEDIA

Studies in this field were begun 10 years ago by one of the present authors and Shaburov [10] and were then continued by Shaburov and Saldadze [12,53,54,95,96]. The principal results of the studies on the thermal stability of anion-exchange resins in mixed and organic media are compiled in Table 4. For comparison, it also includes data characterising the thermal stability of anion-exchange resins in water.

Table 4. Thermal stabilities of anion-exchange resins in mixed and organic media.

Type of anion-exchange resin	Ionic form	DVB content, %	Medium	Temp., °C	Duration of experiment, h	Loss of capacity w.r.t. strongly basic groups, %		References
						by deamination	by degradation	
AV-17	OH	2	H_2O	100	120	6	4	74
ditto	OH	2	CH_3OH	100	120	42	14	74
»	OH	2	C_2H_5OH	100	120	33	9	74
»	OH	6	H_2O	100	120	14	17	10
»	OH	6	50 % CH_3OH	100	120	33	10	10
»	OH	6	75 % CH_3OH	100	120	56	13	10
»	OH	6	CH_3OH	100	120	54	20	12
»	OH	6	C_2H_5OH	100	120	46	18	12
»	OH	16	H_2O	100	120	17	20	74
»	OH	16	CH_3OH	100	120	46	13	74
»	OH	16	C_2H_5OH	100	120	37	16	74
»	Cl	8	H_2O	150	120	29	0	54
»	Cl	8	H_2O	100	120	2	0	54
»	Cl	8	CH_3OH	150	120	62	0	54
»	Cl	8	C_2H_5OH	150	120	70	0	54
»	Cl	8	C_3H_7OH	150	120	76	0	54
»	Cl	8	$C_5H_{11}OH$	150	120	75	0	54
»	Cl	8	$C_{10}H_{21}OH$	150	120	61	0	54
»	OH	6	CH_3COCH_3	100	120	51	23	95
AV-27	OH	8	H_2O	75	120	7	13	13
ditto	OH	8	CH_3OH	75	120	17	29	13
»	OH	8	C_3H_7OH	75	120	11	33	13
AV-16	OH	—	H_2O	150	120	14	72	53
ditto	OH	—	CH_3OH	150	120	10	78	53

The data in Table 4 show that all anion-exchange resins in the OH-form undergo both deamination and degradation, the relative losses of exchange capacity increasing with the concentration of the organic component in the mixed media. In absolute alcohol and acetone, the losses of the exchange capacity of AV-17 anion-exchange resins are much greater than in water. The comparatively low thermal stability of AV-17 anion-exchange resin in alcohols is easily explained by the formation of association complexes of the alcohols with the amino-groups [10,13,54] and in acetone by the polarisation of the C—N bond owing to the participation of the amino-groups in catalysis of the aldol condensation of acetone [95]; all these factors facilitate the elimination of trimethylamine from the matrix. However, the lower thermal stability of the OH- and Cl-forms of the anion-exchange resins in alcohols than in water [13,44,54] is presumably due to the direct chemical interaction between the alcohol molecules and the amino-groups of the anion exchanger catalysed by hydroxide ions. Such interaction with the anion exchanger in the Cl-form leads to deamination via the mechanism [44]

$$RCH_2N(CH_3)_3Cl + R_1OH \rightarrow RCH_2OH + R_1N(CH_3)_3Cl, \quad (21)$$

$$RCH_2N(CH_3)_3Cl + R_1OH \rightarrow RCH_2OR_1 + HN(CH_3)_3Cl. \quad (22)$$

The real composition of the mixture of nitrogen-containing compounds formed as a result of the deamination of AV-17 × 8(Cl) anion-exchange resin in various alcohols at 180°C is presented in Table 5, which shows that the proportion of alkyltrimethylammonium chloride increases with the dimensions of the alcohol molecule, i.e. in parallel with the increased steric hindrance to the formation of ordered solvation shells around the counterions of the functional groups.

Table 5. Composition of the deamination products of AV-17 anion-exchange resin in the Cl-form [97].

Alcohol	Duration of experiment, h	Content, mequiv. g^{-1}		Fraction of alkyltrimethylammonium chloride, %	Loss of capacity, %
		trimethylammonium chloride	alkyltrimethylammonium chloride		
CH_3OH	4	0.84	0.15	15	31
CH_3OH	6	1.00	0.22	18	38
C_2H_5OH	4	0.65	0.12	16	24
C_2H_5OH	6	0.85	0.26	23	35
n-C_3H_7OH	4	0.65	0.23	26	28
n-C_3H_7OH	6	0.75	0.33	30	34
i-C_3H_7OH	6	0.77	0.34	30	34
n-C_4H_9OH	4	0.77	0.32	29	34
n-C_4H_9OH	6	1.11	0.51	32	51
n-$C_5H_{11}OH$	4	0.69	0.37	35	33
n-$C_5H_{11}OH$	6	0.82	0.49	37	41

Deamination of AV-17 anion-exchange resins in the OH-form on interaction with methanol takes place via mechanism (23), as shown by infrared spectroscopy [12]:

$$RCH_2N(CH_3)_3OH + CH_3OH \rightarrow RCH_2OCH_3 + HN(CH_3)_3OH. \quad (23)$$

With increase of the size of the organic group of the alcohol, its reactivity also increases, which leads to a decrease of the thermal stability of AV-17 and AV-27 anion-exchange resins. This correlation, which is in fact between the thermal stability and the positive inductive effect of the aliphatic groups [98], persists only until steric hindrance to the penetration of alcohol molecules into the resin phase appears. When this happens the deamination reactions become more difficult and the thermal stability of anion-exchange resins in alcohols increases after having passed through a minimum [44,54]. A similar relation governs the changes in the losses of exchange capacity as a function of the degree of cross-linking of AV-17 anion-exchange resin. However, in this case it is also necessary to bear in mind the internal concentration of OH^- ions in the resin phase in relation to the sorbed alcohol, which determines (as for cation-exchange resins [99]) the rate of interaction. In particular, the decrease of the thermal stability of the resin with increased content of the cross-linking agent from 2 to 6% is related to this factor [74]. A further increase of the degree of cross-linking to 16% leads to a sharp lowering of the swellability of the resin in alcohols, which causes a corresponding decrease in the concentration of one of the reactants. As a result, the rate of deamination falls despite the increased concentration of OH^- ions relative to the sorbed alcohol. All these factors lead to a higher thermal stability of the anion-exchange resin with 16% DVB compared with less cross-linked specimens.

The relative losses of the capacity of AV-17 anion-exchange resin with respect to the strongly basic groups

in water in the range of cross-linking agent contents investigated (2–16%) are a continuous increasing function of the degree of cross-linking. The difference between this relation and that which has just been discussed for thermal stability in alcohols is undoubtedly due to the higher swellability of the anion-exchange resin in water. As a result, the rate of deamination is determined only by the concentration of the catalytically active OH^- ions in the resin in relation to the bound water, the concentration increasing with the degree of cross-linking.

The electrostatic factors discussed by Shaburov et al.[74] are probably of subsidiary importance.

Degradation involving the residual water [via reaction (12)] is always observed together with deamination when the OH-form of AV-17 anion-exchange resin is heated in alcohols[75]. The absolute decrease of the total exchange capacity of AV-16 and AV-17 anion-exchange resins as a result of their heat treatment in methanol or ethanol exceeds the amount of tertiary amine eliminated[12,13], which indicates the conversion of part of the nitrogen into an inactive state. The mechanism of the reactions occurring under these conditions still requires elucidation.

VI. THE MECHANISM AND KINETICS OF PROCESSES OCCURRING ON HEATING ANION-EXCHANGE RESINS IN WATER AND AQUEOUS ORGANIC AND ORGANIC MEDIA

Earlier it was already stated that the deamination and degradation of the amino-groups of the OH-form of type AV-17 anion-exchange resins are regarded by all investigators as the Hofmann degradation of the quaternary ammonium bases. However, the data in Roginskaya's dissertation[79] and those of other investigators[112], which unfortunately have not been interpreted in sufficient detail, are inconsistent with these ideas and throw doubt on the mechanism adopted for the deamination and degradation of the amino-groups and anion-exchange resins. The following facts are inconsistent with the Hofmann decomposition mechanism.

1. The relative contribution of deamination with a loss of capacity as strongly basic groups on heating the anion-exchange resin in sealed tubes with water falls with increased duration of the experiment, while in a mixed bed and under dynamic conditions it remains unchanged[27,77,79,96].
2. The deamination process terminates long before the strongly basic groups are completely exhausted[27,77].
3. Methanol is evolved in appreciably smaller amounts than that of the weakly basic groups formed[79,112].
4. The content of trimethylamine in the aqueous extract is lower than that of OH^- ions and the deaminated amino-groups formed[79].
5. The unsatisfactory description of the kinetics of the deamination and degradation of the amino-groups by first-order rate equations[75,77,79].
6. The presence of secondary amines among the decomposition products of the anion-exchange resin in the OH-form at 150°C.[77]

We regard the deamination and degradation processes of the amino-groups[100,101] as complex parallel-consecutive reactions involving the nucleophilic substitution of the trialkylamino-group in tetra-alkylammonium by a nucleophilic residue of the molecule of the solvent or the solute, which may consist of products split off from the anion-exchange resin. In these reactions OH^- ions exhibit a catalytic activity[102] and therefore the rate of deamination and degradation of the amino-groups in the OH-form of the anion-exchange resin is much higher than in the Cl-form.

The role of OH^- consists in the activation of the nucleophilic agent as a result of interaction with it. When anion-exchange resins in the OH-form are heated in alcohol, acetone, water, and aqueous solutions of amines the nucleophilic agents are anions (R_1O^-, $CH_3C\lesssim^{CO^-}_{CH_2}$), carbanions ($CH_3COCH_2^-$), hydrated hydroxide ions ($H_2O.OH^-$), and neutral ($R_1-\underset{R_2}{\underset{|}{N}}-R_3$) or hydrated molecules $[(R_1-\underset{R_2}{\underset{|}{NH}}-R_3)OH]$.

In order to understand the chemical reactions of the amino-groups of anion-exchange resins when these are heated in various media, one must take into account the polarisation of the bonds in the amino-group and the resulting induced charges. In the quaternary ammonium groups of AV-17 and AV-27 resins, an induced positive charge arises at the carbon atoms linked to nitrogen as a result of a powerful negative inductive effect[78]. Owing to the influence of the alcoholic hydroxyl, the positive charge induced on the carbon atom of the ethanol group in AV-27 anion-exchange resin is higher than on the other carbon atoms. The presence of an induced positive charge facilitates attack on the carbon atoms by the nucleophilic agent. Each of the carbon atoms linked to nitrogen and the second carbon atom of the ethanol group of AV-27 anion-exchange resin is subject to nucleophilic attack.

Taking into account the foregoing factors, one possible mechanism for the deamination and degradation of the amino-groups of AV-17 anion-exchange resin on heating in sealed tubes with water can be represented schematically by the following reactions[101]:

$$RCH_2\overset{+}{N}(CH_3)_3 + OH^- \rightleftarrows RCH_2N(CH_3)_3OH\ , \qquad (24)$$

$$RCH_2N(CH_3)_3OH + H_2O\cdot HO^- \begin{cases} \rightarrow RCH_2OH + HN(CH_3)_3OH + OH^-\ , & (25) \\ \rightarrow RCH_2NH(CH_3)_2OH + CH_3OH + OH^-\ . & (26) \end{cases}$$

The trimethyl- and benzyldimethyl-ammonium hydroxides evolved are readily dehydrated and converted into tertiary amines:

$$HN(CH_3)_3OH \rightleftarrows H_2O + N(CH_3)_3\ , \qquad (27)$$

$$RCH_2NH(CH_3)_2OH \rightleftarrows RCH_2N(CH_3)_2 + H_2O\ . \qquad (28)$$

Part of the trimethylamine formed dissolves in the aqueous phase and, after Donnan sorption, can participate in the nucleophilic substitution reaction:

$$RCH_2N(CH_3)_3OH + N(CH_3)_3 \rightarrow RCH_2N(CH_3)_2 + N(CH_3)_4OH\ . \qquad (29)$$

When the OH-form of the anion-exchange resin is heated in trialkylamine, the formation of trialkylmethylammonium hydroxide via a reaction of type (29) is probably accompanied also by the substitution of the amino-group of the resin:

$$RCH_2N(CH_3)_3OH + R_1-N\lesssim^{R_3}_{R_2} \rightarrow \left(RCH_2N\lesssim^{R_1}_{R_3}R_2\right)OH + N(CH_3)_3\ . \qquad (30)$$

The above reactions explain some of the contradictions noted above which do not fit within the framework of the old hypotheses. Thus the formation of tetramethylammonium hydroxide via reaction (29) should lead to an increased contribution of the degradation process to the overall loss of capacity by the anion exchanger with increase of the duration of heating and to the appearance of a deficiency of methanol and trimethylamine compared with the content of the weakly basic groups accumulating in the resin and of

OH^- ions in solution. Naturally the deficiency should correspond to the amount of tetramethylammonium hydroxide formed. The cessation of the deamination of strongly basic groups on heating can be explained by postulating that an equilibrium is established between the deamination and amination processes. The amination of the polymeric alcohol produced in reaction (25) by trimethylamine can be represented thus:

$$RCH_2OH + N(CH_3)_3 \rightarrow RCH_2N(CH_3)_3OH\ . \qquad (31)$$

When AV-17 anion-exchange resin is heated in alcohols [101], the following reactions probably occur together with reaction (24):

$$RCH_2N(CH_3)_3OH + R_1O^- \rightarrow RCH_2OR_1 + N(CH_3)_3 + OH^-\ , \qquad (32)$$

$$RCH_2N(CH_3)_3OH + R_1O^- \rightarrow RCH_2N(CH_3)_2 + CH_3OR_1 + OH^-\ . \qquad (33)$$

The involvement of trimethylamine in reactions of types (29) and (31) is in this case less likely than in water owing to its binding by the alcohol molecules into complexes [105].

The heating of AV-17 anion-exchange resins in water under dynamic conditions is accompanied by the removal from the reaction zone of all the products of the conversion of the amino-groups and the processes should be restricted to reactions (25) and (26). In a mixed bed, only trimethylammonium ions are removed, and methanol, which remains partly in the anion-exchanger phase, participates in reactions of types (32) and (33).

The deamination and degradation of AV-17 anion-exchange resin on heating in acetone are due primarily to the interaction of the amino-groups with the solvent and not with the water evolved in the Aldol condensation or contained in the resin. This is confirmed by the much greater losses of capacity by the anion exchanger in acetone than in water. The changes in AV-17 anion-exchange resin in acetone can be represented schematically as follows:

$$CH_3C(O^-)(CH_3)(CH_2) \rightarrow RCH_2OC{=}CH_2 + N(CH_3)_3 + OH^-\ , \qquad (34)$$

$$RCH_2N(CH_3)_3OH + CH_3COCH_2^- \rightarrow RCH_2N(CH_3)_2 + CH_3COC_2H_5 + OH^-\ , \qquad (35)$$

$$RCH_2N(CH_3)_3OH + CH_3COCH_2^- \rightarrow RCH_2CH_2COCH_3 + N(CH_3)_3 + OH^-\ . \qquad (36)$$

When AV-27 anion-exchange resin is heated in water and alcohols the following reactions are likely, disregarding secondary processes involving the products (for example under dynamic conditions):

$$RCH_2N(CH_3)_2OH + H_2O \cdot OH^- \rightarrow RCH_2NH(CH_3)_2OH + HOCH_2CH_2OH + OH^-, \qquad (37)$$

$$RCH_2N(CH_3)_2OH + H_2O \cdot OH^- \rightarrow RCH_2OH + HN(CH_3)_2OH + OH^-\ , \qquad (38)$$

$$RCH_2N(CH_3)_2OH + H_2O \cdot OH^- \rightarrow RCH_2N(CH_3)_3OH + H_2CO + OH^-\ , \qquad (39)$$

$$RCH_2N(CH_3)_2OH + H_2O \cdot OH^- \rightarrow RCH_2NH(CH_3)OH + CH_3OH + OH^-\ , \qquad (40)$$

$$RCH_2N(CH_3)_2OH + R_1O^- \rightarrow RCH_2OR_1 + N(CH_3)_2OH + OH^-\ , \qquad (41)$$

$$RCH_2N(CH_3)_2OH + R_1O^- \rightarrow RCH_2N(CH_3)_2 + R_1OCH_2CH_2OH + OH^+\ , \qquad (42)$$

$$RCH_2N(CH_3)_2OH + R_1O^- \rightarrow RCH_2N(CH_3)CH_2CH_2OH + CH_3OR_1 + OH^-\ . \qquad (43)$$

The first attempts at a kinetic treatment of the experimental decrease of the exchange capacity with respect to strongly basic groups on heating AV-17 and AV-27 anion-exchange resins in the OH-form in water and organic media reduced to the derivation of formal empirical relations of the type $\lg E^{SBG} - f(\lg\tau)$ [13] or to the application of the equation for first-order reactions [75,77,79,106]. We must emphasise that in almost all cases the kinetic curves were found to consist of two sections with different linear slopes. The presence of two stages were explained [10,106] by the energy non-equivalence of the bonds between the amino-groups and the anion-exchanger matrix, while other workers [13,17] suggested that the reaction is inhibited by the deamination product—trimethylamine.

According to Bauman's data [106], the second, slower stage in the decrease of the exchange capacity of Amberlite IRA-400 anion-exchange resin in water is described satisfactorily by a first-order rate law with a 50% conversion time equal to 43 days at 90°C. The authors of later investigations [77,79] adopted the first-order equation for the entire range of deamination and degradation processes involving AV-17 anion-exchange resin in water, but the resulting scatter of the observed rate constants about the mean was unduly great (±60%) and therefore one can hardly regard this attempt as successful.

The change in AV-17 and AV-27 anion-exchange resins in the OH-form on heating in water and ethanol is described satisfactorily by a linear relation between $\lg E^{SBG}$ and $\lg\tau$. [13] However, in acetone the relation becomes more complicated and, when the anion exchanger is re-used, the rate of change of the exchange capacity falls. This feature of the properties of the anion-exchange resin was attributed [95] to its catalytic activity and reactions of the medium.

It follows from the foregoing that the above kinetic equations for the description of the processes involved in the decrease of the exchange capacity of anion-exchange resins are approximate and apply to special cases only.

In recent years a new promising trend appeared in studies on the kinetics of the elimination of functional groups from ion-exchange resins, the principles of which were laid down in a number of investigations [36,37,97,107,108]. The main idea of these studies is that the molecules of the solvent (water or organic liquid) in the solvation shells in the resin phase participate in the process involving the removal of the functional groups. The total amount of solvent in the solvation shells is proportional to the exchange capacity throughout the experiment, since during the heat treatment part of the solvation shell of the functional group split off is removed with it from the resin phase.

The above principles were used in a general treatment of the kinetic data for the deamination of AV-17 anion-exchange resin in the Cl-form, which is the only factor in the decrease of its exchange capacity [54]. Taking into account the foregoing, the rate of deamination in water is defined by the equation

$$-dE/d\tau = k'\,E\,\bar{C}_{H_2O}\ . \qquad (44)$$

Since

$$\bar{C}_{H_2O} = nE\ , \qquad (45)$$

Eqn.(44) is converted into the equation for a reaction which is second-order with respect to the concentration of the functional groups:

$$-dE/d\tau = k'E^2n = kE^2, \qquad (46)$$

where n is the solvation number of the functional group (mmoles H_2O mequiv.$^{-1}$). Under the initial conditions ($\tau = 0$, $E = E_0$),

$$E = E_0/(1 + kE_0\tau). \qquad (47)$$

The agreement between the experimental data for the deamination of AV-17 anion-exchange resin in the Cl-form

and the values calculated by Eqn.(47) has been demonstrated convincingly[107]. The temperature variations of the apparent rate constant for the deamination reaction obeys the Arrhenius equation quite satisfactorily with a pre-exponential factor of $(4.3 \pm 0.1) \times 10^{17}$ kg matrix mole^{-1} h^{-1} and an activation energy of 40.2 ± 0.2 kcal mole^{-1}.

The mechanism[44] and kinetics of the processes occurring[107] change with decrease of the water content of the anion-exchange resin, deamination being supplemented by degradation.

A detailed study of the kinetics of the deamination of AV-17 anion-exchange resin in the Cl-form in alcohols has been made[97]. It might have been expected that in alcohols, as in water, the deamination of the Cl-form of the resin could be described by the equation for second-order reactions. This is indeed the case for all the alcohols except methanol[97]. The kinetics of the deamination of AV-17 anion-exchange resin in methanol obey a first-order rate law. Evidently in this case the effect of the high affinity of methanol for the active groups operates, as a result of which the nucleophilic substitution reaction involves the same mechanism as under homogeneous conditions. The amount of trimethylammonium chloride[97] varies with time according to a curve with a maximum, which indicates its consecutive transformation via the reaction

$$HN(CH_3)_2Cl + CH_3OH \rightarrow N(CH_3)_4Cl + H_2O \ . \qquad (48)$$

This concept is fully consistent with the correspondence of the overall content of nitrogen-containing compounds in the resin decomposition products both to the loss of exchange capacity and to the total amount of Cl^- ions in the liquid phase. Bearing in mind that the kinetics of reaction (48) are described by a first-order equation[109] the decrease of the exchange capacity of AV-17 anion-exchange resin (E) in methanol via reactions (21) and (22) and of the accumulation of trimethylammonium (C_1) and tetramethylammonium (C_2) chlorides is described[97] by the equations

$$-dE/d\varepsilon = (k_1 + k_2)E \ , \qquad (49)$$

$$dC_1/d\tau = \frac{k_1^2}{k_1 + k_2} \cdot E - k_3 C_3 \ , \qquad (50)$$

$$dC_2/d\tau = \frac{k_2}{k_1 + k_2} \cdot E + k_3 C_1 \ , \qquad (51)$$

where k_1, k_2, and k_3 are the apparent rate constants for reactions (22), (21), and (48). For the initial conditions ($\tau = 0$, $E = E_0$, $C_1 = 0$, and $C_2 = 0$), the solution of Eqns. (49)–(51) is

$$E = E_0 \cdot \exp[-(k_1 + k_2)\tau] \ , \qquad (52)$$

$$C_1 = \frac{k_1^2 E_0}{(k_1 + k_2)(k_1 + k_2 - k_3)} \{\exp(-k_3\tau) - \exp[-(k_1 + k_2)\tau]\} \ , \qquad (53)$$

$$C_2 = \frac{E_0}{(k_1 + k_2)} \left\{ \frac{k_1^2}{(k_1 + k_2 - k_3)} [1 - \exp(-k_3\tau)] - \left[\frac{k_1^2 \cdot k_3}{(k_1 + k_2)(k_1 + k_2 - k_3)} + \frac{k_2^2}{(k_1 + k_2)} \right] [1 - \exp[-(k_1 + k_2)\tau]] \right\} \ . \qquad (54)$$

The apparent rate constants for the above reactions at different temperatures and the results of calculations using the Arrhenius equationare presented in Table 6.[97]

The subscripts 1, 2, and 3 to the symbols k, ΔU, and A show that they refer to reactions (22), (21), and (48) respectively.

More complete information about the process kinetics on heating anion-exchange resins in the OH-form may be obtained taking into account the mechanism proposed[101] and the characteristics of the behaviour of the swollen resin. The resin is then regarded[111] as a pseudohomogeneous system consisting of the hydrocarbon matrix, fixed ions, counterions, hydration (solvation) shells, and the molecules sorbed from the external solution. During the heat treatment, the ions and molecules sorbed by the resin phase (by the hydration shells) are expelled from it by the elastic forces of the matrix together with the functional groups eliminated and the hydration shells. Thus during the heat treatment of the resin, the content of all the components, except the weight of the matrix, changes. Hence it follows that, in calculations on the kinetics of the elimination of functional groups from resins, the method of expressing the concentrations of the remaining components per litre of the solvent, which is generally adopted in physical chemistry, is inapplicable and the method proposed previously[37] in which they are referred to 1 g (1 kg) of the matrix treated formally as a "solvent" is the most reliable. The dilution of the mobile counterions and sorbed molecules by the solvent in the resin phase is then taken into account by the molality $\bar{m} = \bar{C}d_S/\bar{C}_S\epsilon_S$, where $\bar{C}$ and $\bar{C}_S$ are the concentrations of the dissolved component and the solvent in the resin phase [mequiv. (mmole)/g matrix] and d_S and ϵ_S are the density and the molecular weight of the solvent.

Table 6. Kinetic parameters of reactions (22), (21), and (48) in methanol[97].

Temp., °C	Reaction rate constant, h^{-1}			Activation energy, kcal mole^{-1}	Pre-exponential factor in Arrhenius equation, h^{-1}
	10^2k_1	10^2k_2	10^2k_3		
160	3.66±0.08	0.79±0.06	2.70±0.06	$\Delta U_1 = 35$	$A_1 = 1.2 \cdot 10^{16}$
170	7.6 ±0.2	2.14±0.14	5.45±0.17	$\Delta U_2 = 40$	$A_2 = 6.0 \cdot 10^{17}$
180	20.0 ±1.4	6.3 ±0.5	10.7 ±0.8	$\Delta U_3 = 26$	$A_3 = 4.1 \cdot 10^{11}$

Taking into account reactions (24)–(27), (29), and (31) and the analogies with the treatment of Tulupov and Shaburov[101], the kinetics of the processes involving the decrease of the exchange capacity with respect to strongly basic groups (E^{SBG}), deamination (q_1), and degradation (q_2) of AV-17 anion-exchange resin on heating with water in sealed tubes are described by the following equations:

$$-dE^{SBG}/d\tau = (k'_{25} + k'_{26})\bar{C}_b\bar{C}_a/\bar{C}_{H_2O} + k'_{29}\bar{C}_b\bar{C}_e/\bar{C}_{H_2O} - k'_{31}\bar{C}_f\bar{C}_e/\bar{C}_{H_2O}, \qquad (55)$$

$$dq_1/d\varepsilon = k'_{25}k'_{26}\bar{C}_b\bar{C}_a/\bar{C}_{H_2O}(k'_{25} + k'_{26}) - k'_{31}\bar{C}_f\bar{C}_e/\bar{C}_{H_2O} \ , \qquad (56)$$

$$dq_2/d\tau = k'_{26}k'_{26}\bar{C}_b\bar{C}_a/\bar{C}_{H_2O} + k'_{29}\bar{C}_b\bar{C}_e/\bar{C}_{H_2O} \ . \qquad (57)$$

The material balance equation is

$$E_0^{SBG} = E^{SBG} + q_1 + q_2 \ . \qquad (58)$$

Assuming that the strongly basic groups of the anion-exchanger are fully dissociated, like alkalis of the NaOH type, and that $\bar{C}_{RCH_2\dot{N}(CH_3)_3} = E^{SEG}$, Eqns.(55)–(57) can be reduced to the following form by simple rearrangements:

$$-dE^{SBG}/d\tau = (k''_{25} + k''_{26})(E^{SBG})^2(1 + \alpha)\bar{m}_{OH^-} + k''_{29}E^{SBG}\bar{m}_e\bar{m}_{OH^-} - k''_{31}(E^{SBG})^2 \cdot \bar{m}_{OH^-}\bar{m}_e \ , \qquad (59)$$

$$dq_1/d\tau = \frac{k''_{25} \cdot k''_{26}}{k''_{25} + k''_{26}}(E^{SBG})^2(1 + \alpha)\bar{m}_{OH^-} - k''_{31}(E^{SBG})^2\bar{m}_e\bar{m}_{OH^-}(1 + \alpha) \ , \qquad (60)$$

$$dq_2/d\tau = \frac{k''_{29} \cdot k''_{26}}{k''_{25} + k''_{26}}(E^{SBG})^2(1 + \alpha)\bar{m}_{OH^-} + k''_{29}(E^{SBG})\bar{m}_e\bar{m}_{OH^-} \ . \qquad (61)$$

The following notation is employed: $a = H_2O.OH^-$; $b = RCH_2N(CH_3)_3OH$; $e = N(CH_3)_3$; $f = RCH_2OH$; $g = RCH_2\overset{+}{N}(CH_3)_3$; α = content (mmole mequiv.$^{-1}$) [108] of tetramethylammonium hydroxide in the hydration shell of the functional group sorbed by the Donnan mechanism;

$$k''_{25} = k'_{25}K_{24}K_e \cdot 55{,}5\,\bar{\gamma}_g\bar{\gamma}^2_{OH^-}/\bar{\gamma}_a\bar{\gamma}_b;\ k''_{26} = k'_{26}k''_{25}/k'_{25},$$
$$k''_{29} = k'_{29}K_{24} \cdot 55{,}5^2\bar{\gamma}_g\gamma_{OH^-}/\gamma_{H_2O}\bar{\gamma}_b;\ k''_{31} = k'_{31}k'_{25}k''_{25}/(k'_{25} + k'_{26}).$$

The numerical subscript to the rate constant k or the equilibrium constant K corresponds to the number of the reaction, K_e is the equilibrium constant for the hydration of hydroxide ions, γ is the activity coefficient, and a bar over a symbol implies that it refers to the resin phase.

The solution of Eqns. (59)–(61) involves considerable difficulties, since the molalities of the hydroxide ions and trimethylamine in the resin phase vary continuously as the deamination and degradation of the anion-exchange resin proceed.

The molality of trimethylamine in the resin phase found from the Donnan equilibrium [110] depends on the proportions of the external solution and the resin in the experiment and on the solubility of trimethylamine in the external solution:

$$\bar{m}_e = \frac{-0.018E^{SBG}}{2\bar{C}_{H_2O}} + \sqrt{\left(\frac{0.018E^{SBG}}{2\bar{C}_{H_2O}}\right)^2 + \beta\frac{0.018C_e}{C_{H_2O}}} \quad (62)$$

As the limiting solubility of triethylamine in the external solution is approached, its molality in the resin phase will tend to a constant value. The molality of OH^- ions in the anion-exchange phase is determined by the capacity for hydration of the strongly basic amino-groups† and tetramethylammonium hydroxide sorbed as a result of the Donnan distribution:

$$\bar{m}_{OH^-} = \frac{0.018E^{SBG}}{2\bar{C}_{H_2O}} + \sqrt{\left(\frac{0.018E^{SBG}}{2\bar{C}_{H_2O}}\right)^2 + \beta_1\frac{0.018C_{N(CH_3)_4OH}}{C_{H_2O}}}, \quad (63)$$

where β and β_1 are the ratios of the activity coefficients of trimethylamine and tetramethylammonium hydroxide in the resin phase and in the external solution.

As tetramethylammonium hydroxide accumulates, the molality of OH^- ions in the resin phase and the rates of the deamination and degradation processes should increase. However, in the presence of a large excess of "external" water and also on heating the anion-exchange resin under dynamic conditions and in a mixed bed, the Donnan sorption of trimethylamine and tetramethylammonium hydroxide may be neglected. In such experiments the contribution of reactions (29) and (31) to the decrease of the exchange capacity of the anion exchanger will be reduced to a minimum and Eqns. (59) to (61) simplify to

$$-dE^{SBG}/d\tau = (k'_{25} + k'_{26})(E^{SBG})^2\bar{m}_{OH^-}, \quad (64)$$

$$dq_1/d\tau = \frac{(k'_{25})^2}{(k'_{25} + k'_{26})} \cdot (E^{SBG})^2\bar{m}_{OH^-}, \quad (65)$$

$$dq_2/d\tau = (k'_{26})^2(E^{SBG})^2\bar{m}_{OH^-}/(k'_{25} + k'_{26}). \quad (66)$$

The change in the molality of OH^- ions in the anion-exchanger phase during the experiment may be neglected (as in experiments with cation exchange resins [111]) and, having assumed that the activity coefficient ratio in the resin is constant, we obtain the following solution of Eqns. (64)–(66) for the initial conditions ($\tau = 0$, $E^{SBG} = E^{SBG}_0$, $q_1 = q_2 = 0$):

$$E^{SBG} = E^{SBG}_0/[1 + (k_{25} + k_{26}) \cdot E^{SBG}_0 \cdot \tau], \quad (67)$$

$$q_1 = k_{25} \cdot E^{SBG}_0/[k_{25} + k_{26} + 1/\tau \cdot E^{SBG}_0], \quad (68)$$

$$q_2 = k_{26} \cdot E^{SBG}_0/[k_{25} + k_{26}) + 1/\tau \cdot E^{SBG}_0], \quad (69)$$

where $k_{25} = k'_{25}\bar{m}_{OH^-}$ and $k_{26} = k'_{26}\bar{m}_{OH^-}$ are the apparent rate constants for the deamination and degradation of the anion exchanger amino-groups.

One must note that Eqns. (67)–(69) make it possible to carry out calculations on the process kinetics even when there are difficulties in the determination of the molality of OH^- ions (macroporous and condensation resins) or in the interpretation of published experimental data containing insufficient information about the capacity of the functional groups for hydration. In such cases one can find the constant k, which includes the molality of hydroxide ions.

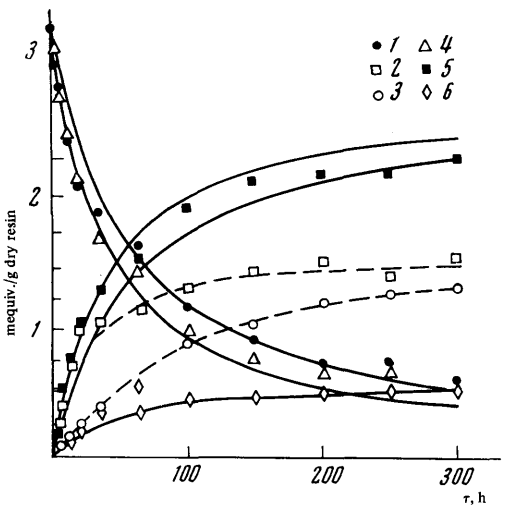


Figure 1. Decrease of E^{SBG} (*1* and *4*), deamination (*2* and *5*), and degradation (*3* and *6*) of the amino-groups of AV-17 anion-exchange resin in the OH-form at 125°C in water (*1*–*3*) and in a mixed bed (*4*–*6*). The continuous curves have been calculated by Eqns. (67)–(69) and the dashed curves have been drawn on the basis of the experimental data; points *1*–*6* have been taken from Roginskaya' et al. [27]

Thus interpretation of the experimental results obtained on heating AV-17 anion-exchange resin under dynamic conditions [98] and in a mixed bed [27] demonstrated the satisfactory applicability of Eqns. (67)–(69). The discrepancy between the experimental and calculated data for high degrees of decomposition of the amino-groups of AV-17 anion-exchange resin in a mixed bed is due to the conversion of the functional groups from the OH-form into the sulphate-form as a result of the neutralisation of the sulphuric acid evolved on desulphonation of KU-2 cation-exchange resin [27]. Reactions (29)–(31) have a compensating effect on the decrease of E^{SBG} and therefore, even when the anion-exchange resin is heated with water in sealed tubes, there is a satisfactory agreement between the experimental data and the values calculated by Eqn. (67) (Fig. 1).

† The dissociation of the weakly basic groups is neglected.

The deamination and degradation curves calculated by Eqns.(68) and (69) did not then of course coincide with the experimental curves, since the contributions of the second terms in Eqns.(56) and (57) cannot be neglected. The contribution of reactions (29) and (31) to the deamination and degradation processes increases with the duration of heating and also with decrease of the degree of cross-linking of the matrix and of the ratio of the volumes of the external solution and the resin in the experiment. In studies by Shaburov and coworkers [13,74,75], the relative content of water was probably significantly higher than in the work of Roginskaya and coworkers [27] and therefore in the first case even deamination and degradation of amino-groups are frequently described satisfactorily by Eqns.(68) and (69). This can be illustrated by the data in Fig. 2.

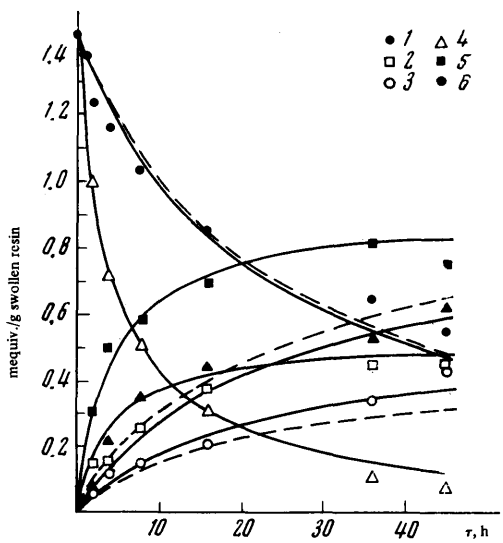


Figure 2. Decrease of E^{SBG} (*1* and *4*), deamination (*2* and *5*), and degradation (*3* and *6*) of the amino-groups of AV-17 × 6 anion-exchange resin in the OH-form on heating in water at 135°C (*1–3*) and 150°C (*4–6*). The continuous and dashed curves have been calculated by Eqns.(67)–(69) and (67)–(71) respectively. The experimental points have been taken from Shaburov [75].

The sum of the apparent rate constants $k_{25} + k_{26}$ was found from the relation $1/E^{SBG} - 1/E_0^{SBG} = (k_{25} + k_{26})\tau$. The constants k_{25} and k_{26} were found from the sum of the constants and the contributions of the deamination and degradation processes under the initial conditions when reactions (29) and (31) may be neglected. The rate constants calculated by this method, the ranges of variation of the exchange capacity at different temperatures, and the calculated exchange capacities E_0^{SBG} (in mequiv./g matrix) (from the formulae in Table 1) are listed in Table 7.

The data in Table 7 show that the deviations from the mean values of the apparent rate constants for the deamination and degradation of the amino-groups found with the aid of the equations proposed amount to 10–25% and are appreciably smaller than those found using the equations for first-order reactions (±60%). [77,79] This finding is undoubtedly evidence in support of the new principles underlying the treatment of the thermal stability of the functional groups of ion-exchange resins.

One must note that in the kinetic treatment of published data about 13% of amino-groups, which were split off in water and alcohols at an appreciably higher rate than the remaining groups, were detected only for the anion-exchanger specimen with 16% DVB.

Table 7. Apparent rate constants for the deamination (k_{25}) and degradation (k_{26}) of the amino-groups of anion-exchange resins on heating in water.

Type of anion-exchange resin	Temp., °C	Exchange capacity, mequiv. g^{-1} in text E_0^{SBG}	in text E_f^{SBG}	$E_d^{M,SBG}$, mequiv. /g matrix	Rate constants, kg matrix $mole^{-1}$ h^{-1} 10^3k_{25}	10^4k_{26}	References
AV-17 × 6[a] (OH)	85	4.03	3.24	5.90	7.8 ±1.3	0.16±0.03	79
	103		2.62		0.24±0.04	0.7 ±0.12	79
	118		0.42		2.7 ±0.2	11.0 ±0.9	79
	140		0.08		8 ±2	55.0 ±13	79
AV-17 × 8[a] (OH)	90	3.26	1.80	4.38	0.21±0.02	1.1±0.1	77
	110		0.67		1.04±0.1	6.2±0.6	77
	116		0.83		1.9 ±0.3	8 ±1	79
	125		0.26		7.1 ±0.9	44 ±5	79
	116[d]		0.84		2.8 ±0.3	13 ±2	27
	125[d]		0.52		3.9 ±0.5	18 ±2	27
AV-17 × 2[b] (OH)	100	1.10	0.97	5.67	0.1 ±0.02	0.7±0.2	74
AV-17 × 6[b] (OH)	75	1.44	1.32	5.00	0.016±0.003	0.13±0.03	75
	100		1.09		0.22±0.05	1.5±0.3	13
	120		0.69		1.07±0.03	7.7±0.2	75
	135		0.56		5.0 ±1.0	40 ±7	75
	150[c]		0.07		277 ±10	2000±70	75
	75[e]		1.15		0.33±0.002	0.9±0.01	96
	90[e]		1.09		0.46±0.1	1.16±.024	96
AV-17[a] (Cl)	150	3.72	2.41	5.65	0.50±0.07		74
	160	3.20	0.77	4.57	2.2 ±0.2		97
	170		0.98		6.1 ±0.2		97
	180	2.96	1.11	4.23	16.6 ±0.8		97
AV-17 × 16[b] (OH)	100	1.56	0.98	2.97	0.44 ±0.01	2.8±0.1	74
AV-27[b] (OH)	75	1.57	0.93	5.50	0.215±0.003	3.1±0.03	13
	100		0.17		3.2 ±0.5	57 ±9	13

[a]The exchange capacity was quoted in the original paper in mequiv./g dry resin. [b]The exchange capacity in the original paper was quoted in mequiv./g swollen resin. [c]These constants in the Arrhenius equation correspond to $t = 190°C$. [d]The resin was heated in a mixed bed with KU-2 cation-exchange resin in the H-form. [e]The resin was heated under dynamic conditions.

The kinetic parameters in the Arrhenius equation obtained for the experiments in water on the basis of the data of Shaburov and coworkers [75] and Roginskaya and coworkers [77] are virtually identical. Thus the deamination of AV-17 × 6 (Shaburov [75]) and AV-17 × 8 (Roginskaya et al. [77]) anion-exchange resins in water is characterised by activation energies of 27 ± 2 and 26 ± 3 kcal $mole^{-1}$ and pre-exponential factors of (3.9 ± 2.5) × 10^{12} and (1.2 ± 0.2) × 10^{12} kg matrix $mole^{-1}$ h^{-1}; the corresponding parameters for their degradation are 26 ± 6 and 25 ± 3 kcal $mole^{-1}$ and (8.5 ± 6.3) × 10^{11} and (9.9 ± 3.6) × 10^{11} kg matrix $mole^{-1}$ h^{-1} respectively.

Eqns. (67)–(69) can be successfully extended to other media. Thus their use yielded satisfactory results for experiments in which AV-17 anion-exchange resin was heated not only in alcohol but also in aqueous alcoholic media and in acetone, as shown by the slight scatter of the apparent rate constants about the mean (Table 8) and the satisfactory agreement between the calculated and experimental kinetic curves (Fig. 3).

Table 8. Apparent rate constants and the contribution of deamination to the loss of capacity of anion-exchange resins in the OH-form at 100°C in organic media and aqueous methanol.

Anion-exchange resin	Medium	Deamination, %	Rate constant, 10^4 kg matrix mole^{-1} h^{-1}		References
			deamination k_{32}	degradation k_{23}	
AV-17 × 2	CH_3OH	74±4	11±1	6.5±0.5	74
AV-17 × 6	50 % CH_3OH	76±1	11±8	6.5±4.7	75
AV-17 × 6	75 % CH_3OH	78±2	16±3	8.4±1.3	75
AV-17 × 6	CH_3OH	75±3	27±2	16 ±1	75
AV-17 × 6	C_3H_7OH	86±3	11±2	4.4±1	13
AV-17 × 6	$C_5H_{11}OH$	69±1	26±5	17 ±3	13
AV-17 × 6	CH_3COCH_3	70±9	5±1*	3.6±0.8**	95
AV-17 × 16	CH_3OH	76±3	29±4	17 ±2	74
AV-27	CH_3OH	38±1	180±30	220 ±40	13
AV-27	CH_3COCH_3	27±1	53±19*	87 ±31**	94

Note. In acetone, the deamination (*) and degradation (**) constants are $k_{34} + k_{36} + k_{35}$ respectively.

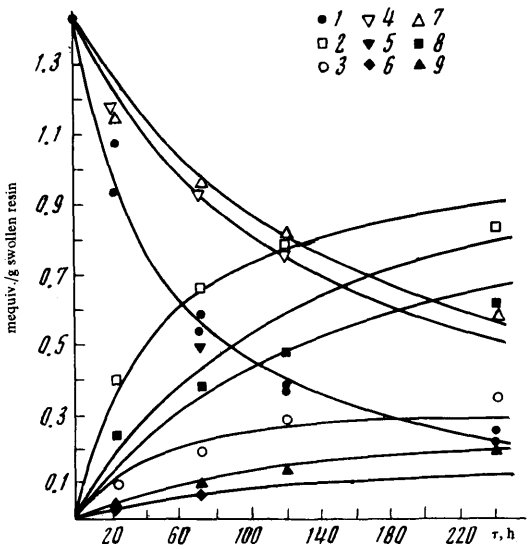


Figure 3. Decrease of E^{SBG} (*1*, *4*, and *7*), deamination (*2*, *5*, and *8*), and degradation (*3*, *6*, and *9*) of the amino-groups of AV-17 × 6 anion-exchange resin in the OH-form at 100°C in methanol (*1–3*), pentanol (*4–6*), and 50% aqueous methanol (*7–9*). The curves have been calculated by Eqns. (67)–(69); the experimental points *1–9* have been taken from Shaburov and coworkers [13,75].

According to Shaburov [75], in ethanol the deamination process has an activation energy of 28 ± 2 kcal mole^{-1} and a pre-exponential factor of (5.2 ± 0.6) × 10^{13} kg matrix mole^{-1} h^{-1}; the corresponding parameters for its degradation are 28 ± 3 kcal mole^{-1} and (2.6 ± 0.4) × 10^{13} kg matrix mole^{-1} h^{-1}.

Despite the expected wide variety of reactions on heating AV-27 anion-exchange resin, the overall processes involving a decrease of E^{SBG}, deamination, and degradation are satisfactorily described by Eqns. (67)–(69) in all the media investigated, as shown by the small deviations of the rate constants from the mean values (Tables 7 and 8) and by the satisfactory agreement between the experimental points and the calculated kinetic curves (Figs. 4 and 5).

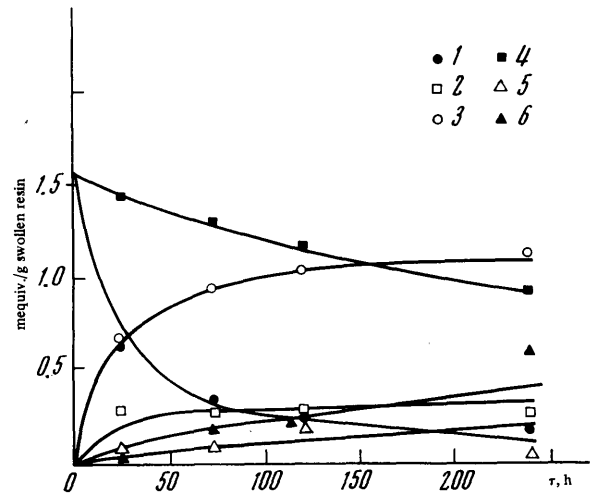


Figure 4. Decrease of E^{SBG} (*1* and *4*), deamination (*2* and *5*), and degradation (*3* and *6*) of the amino-groups of AV-27 anion-exchange resin in the OH-form in water at 100°C (*1–3*) and 75°C (*4–6*). The curves have been calculated by Eqns. (67)–(69); the experimental points *1–6* have been taken from Shaburov and Saldadze [13].

Eqns. (67)–(69) show that there should be a direct proportionality between the apparent rate constants for deamination and degradation and the molality of OH^- ions in the anion-exchanger phase in relation to the sorbed solution for resins with different contents of the cross-linking agent. The molalities of hydroxide ions in AV-17 resin specimens with 2.6 and 16% DVB calculated from the initial equivalent coefficients of moisture absorption capacity quoted by Shaburov et al. [74] are 1.52, 2.41, and 4.34 equiv.OH^-/litre water.

The linear relation between the constants k_{25} and k_{26} and the pre-exponential factors in the Arrhenius equation on the one hand and the molality of the hydroxide ion in the anion-exchanger phase on the other (Fig. 6) leads to a realistic method for the theoretical calculation of the thermal stability of the resins in water at any temperature. A similar relation was found earlier also for sulphonic acid cation-exchange resins [111].

The apparent rate constants for the deamination and degradation of the amino-groups may be calculated from equations which follow from Fig. 6:

$$k_{25} = (3.51 \cdot \bar{m}_{OH^-} - 2.50) \cdot 10^{12} \cdot \exp(-28 \cdot 10^3/RT) , \quad (70)$$

$$k_{26} = (1.36 \cdot \bar{m}_{OH^-} - 0.40) \cdot 10^{12} \cdot \exp(-28 \cdot 10^3/RT) . \quad (71)$$

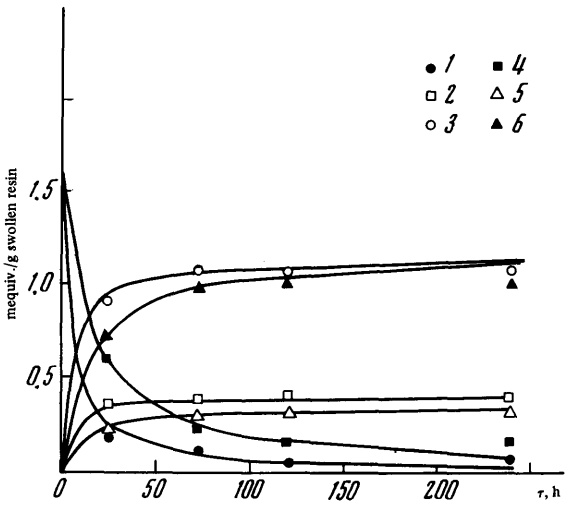


Figure 5. Decrease of E^{SBG} (*1* and *4*), deamination (*2* and *5*), and degradation (*3* and *6*) of the amino-groups of AV-27 anion-exchange resin in the OH-form at 100°C in ethanol (*1*–*3*) and pentanol (*4*–*6*). The curves have been calculated by Eqns. (67)–(69); the experimental points *1*–*6* have been taken from Shaburov and Saldadze [13].

The applicability of Eqns. (70) and (71) combined with Eqns. (67)–(69) for the calculation of the curves describing the decrease of E^{SBG}, deamination, and degradation may be illustrated by the data presented in Fig. 2 for experiments in which AV-17 anion-exchange resins were heated in water at 135°C.

The present stage in the development of studies on the thermal stability of anion-exchange resins is characterised by an endeavour on the part of investigators to extend the range of instrumental methods for the solution of many problems concerning not only the fate of the functional groups but also the changes in the matrix itself; they will provide a key to the creation of mechanically stable ion-exchange resins.

Another characteristic feature of such studies is an endeavour to unify and standardise the research techniques. Unfortunately little has yet been done in this important field.

A third and most important feature of the present stage in the development of studies on the thermal stability of resins is the concentration of the efforts of investigators on the elucidation of the mechanisms of processes involving the elimination of functional groups. The results presented in this review have demonstrated quite clearly the effect of the medium and its capacity to undergo changes under the influence of the anion-exchange counterions on the stability of the functional groups of the resin itself. This view concerning the relation between the catalytic activity and thermal stability of sulpho-groups was formulated in the previous review [1] and in this review has been developed further and given a more clear-cut theoretical basis.

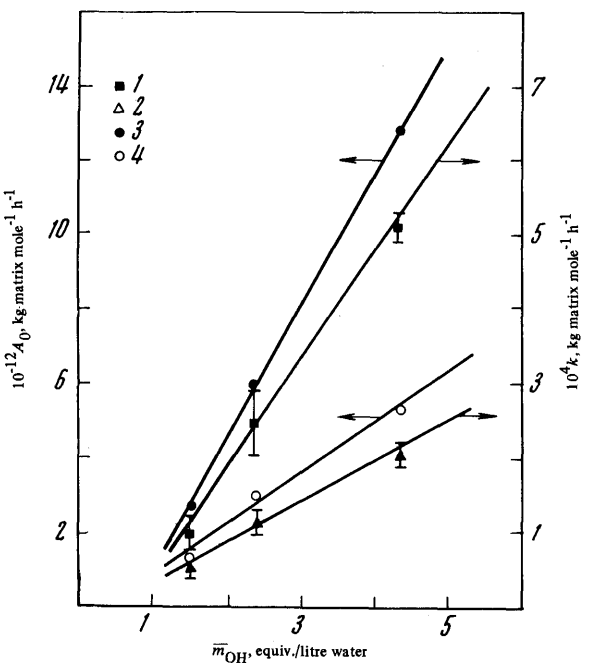


Figure 6. Variation of the apparent rate constants k at 100°C (*1* and *2*) and the pre-exponential factors A_0 in the Arrhenius equation (*3* and *4*) for the deamination (*1* and *3*) and degradation (*2* and *4*) of the amino-groups of AV-17 anion-exchange resin in water as a function of the molality of OH^- ions in the resin phase (points *1*–*4* have been obtained from the data of Shaburov et al. [74]).

The endeavour by investigators to give a mathematical description of the conversion of functional groups on the basis of a kinetic approach we believe to deserve all possible encouragement and further development.

The new ideas about the mechanisms of the deamination and degradation of anion-exchange resins in which the bond polarisation in the unit cell and the involvement of OH^- ions as reaction catalysts in the formation of intermediates are taken into account may not correspond to the true situation in all details and in this sense remain controversial. However, the fruitfulness of this approach is evident. With its aid, kinetic equations have been obtained giving a satisfactory description of earlier experimental data and allowing theoretical calculations, based on the known exchange capacities and molalities of the counterions in the resin phase, on the kinetics of the decrease of the content of strongly basic groups, deamination, and degradation of anion-exchange resins at any temperature. There is no doubt that further development

of studies in the field of the thermal stability of ion-exchange materials and (as model substances) of their low-molecular-weight analogues will create firm foundations for the synthesis of such materials in which the structural elements will be correctly combined and new resins with satisfactory operational properties will be created.

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Karpov Physicochemical Institute, Moscow

Tambov Institute of Chemical Machine Engineering

U.D.C. 547.451

Organophosphorus Fungicides

A.F.Grapov and N.N.Mel'nikov

The review examines the applications of organic derivatives of phosphorus as agricultural fungicides. Trends in the development of research in this field have been noted and data are presented on the mechanism of the action of certain preparations. The bibliography includes 263 references.

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I. INTRODUCTION

The use of organic derivatives of phosphorus as fungicides and herbicides constitutes a new and promising field of their application in the national economy [1-8]. The first studies in which the microbiological action of organic derivatives of phosphorus was noted were made at the beginning of the 1940's, but systematic investigations of their fungicidal and bactericidal properties were begun much later [9-11]. By 1972, 450 publications had been devoted to organophosphorus fungicides, some preparations found practical application, and others are being tested as experimental fungicides.

At the present time the main advances in the field of phosphorus-containing fungicides have been made in combating diseases of rice caused by the fungi *Piricularia* and *Pellicularia sasaki*. The reduction of the rice crop due to infection by *Piricularia* in the countries of South East Asia reaches 10%. As a result of vigorous measures taken to protect rice from disease, the losses in Japan have been reduced to 3%. Nevertheless they have been estimated at 250 000–350 000 tons of rice per year in an overall crop of 12–14 million tons [12,13].

The main preparations for the treatment of the infection of rice by Piricularia in Japan are phosphorus-containing fungicides (kitazin, kitazin P, inezin, hinosan, and cerezin) and antibiotics (kasugamycin and blasticidin). The industrial manufacture of these preparations was begun in 1966 [14] and in 1970 the manufacture of kitazin and kitazin P reached a total output of 1600 tons and that of hinosan 700 tons.

Phosphorus compounds with microbiological activities have a wide variety of chemical properties. Among these one encounters potential alkylating, acylating, and phosphorylating agents, oxidants, reductants, and complex-forming agents. These findings show that their action on the fungal cell is not unambiguous.

The advances in the chemistry of organic phosphorus-containing insecticides are in many ways related to the creation of a reliable model of the mechanism of the insecticidal action. For the mechanism of the fungicidal action, such a model has not been established so far. In view of the different types of action of organophosphorus preparations on the fungal cell, it is probably necessary to develop not one but several models. Unfortunately there have been virtually no biochemical studies on the action of phosphorus-containing preparations on processes in the fungal cell.

The bulk of the information on the fungicidal action of organic derivatives of phosphorus is concentrated in patent publications. The present review covers only the literature for the period 1967–1971 inclusive, since earlier studies on this question have been examined in a previous review [4].

II. DERIVATIVES OF PHOSPHOROUS AND PHOSPHINOUS ACIDS

The fungicidal and bactericidal activities of phosphorus(III) derivatives are probably associated with their reducing properties [4]. Dialkyl-, dicyclohexyl-, diphenyl-, and di(phenylethyl)-phosphinites exhibit bactericidal and bacteriostatic activities [15,16]. Cyclohexylammonium, piperidinium, and furfurylammonium salts of *O*-methyl- and *O*-phenyl-phosphorous acids also show germicidal properties [17]. It has likewise been noted that triaryl, tri(naphthylmethyl), and tri-(α-cyanopentachlorobenzyl) phosphites [19,20,21], dinitrophenyl phenylene phosphites [22], and a mixture of β-aminoethyl phosphite and *N*-β-hydroxyethyl phosphoramidite, obtained from *OO*-dimethylphosphorous acid and monoethanolamine [18], exhibit a high fungicidal activity against phytopathogenic fungi and also as antiseptics for the protection of wood.

The anhydrides of phenylphosphonous and arenesulphonic acids and dialkyl trimethylstannyl phosphites have been patented as agents effective against *Pellicularia sasaki* on rice [23,24].

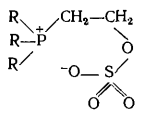
III. PHOSPHINES AND PHOSPHONIUM SALTS

Substituted phosphines show a low fungicidal activity. Chlorotri(diphenylphosphino)methane at a concentration of 30–100 mg litre^{-1} destroys the spores of *Venturia inaequalis* on apple seedlings [25]. Trialkylstannylhydroxyethyldialkylphosphines have been patented as germicidal preparations [26].

Trialkylbenzylphosphonium, triarylbenzylphosphonium, tetra-(α-hydroxybenzyl)phosphonium, and tetra(arylamino)phosphonium salts suppress the growth of pathogenic micro-organisms much more effectively than

phosphines and aminophosphines [27-31]. Thus trialkylbenzylphosphonium salts suppress the growth of the spores of *Alternaria solani*, *Monilinia fructicola*, and *Stemphylium sarcinaeforme* and are effective against anthracnose and tomato blights [29]. The structure of both the cationic and anionic components of the molecule has a marked influence on its activity and the selectivity of its action. For example, alkyltriphenylphosphonium phosphorothioates and phosphorodithioates are several times as effective as the corresponding salts with inorganic anions in their action on the fungi *Alternaria* and *Botrytis* [30]. The considerable phytocidal activity of the preparations, which limits the scope of their application in plant cultivation, must be regarded as a disadvantage of this group of compounds [4].

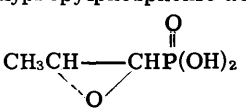
Phosphonium zwitterions, obtained by the reaction of trialkylphosphines with cyclic sulphates, suppress the growth of *Bacillis subtilus* and *Pullularia pullulans* [32].



IV. ACIDS OF TETRACOORDINATE PHOSPHORUS AND THEIR SALTS

O-Alkyl-, *O*-aryl-, and *OO*-diaryl-phosphorous acids and their salts show a moderate fungicidal activity against the fungi *Fusarium*, *Phytophthora*, *Pythium*, and *Aspergillus* [33-36]. For example, *O*-(1-diethylamino-2-propyl)*O*-dodecylphosphorous acid protects cucumber plants from mildew under greenhouse conditions at a dose of 2 kg per hectare [32]. The salts of alkylaminomethylphosphonic, *N*-substituted *O*-(α-aminobenzyl)phosphoric, phosphanilic, and difluorophosphanilic acids as well as laurylammonium *N*-laurylchloromethylphosphonamidate have been patented as germicides [37-39].

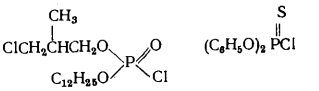
Studies on the microbiological activities of 1,2-epoxypropylphosphonic acid and its salts have been made in the laboratories of the Merck Company. The acid itself at a concentration of 0.01% completely suppresses the growth of the spores of *Macrosporium sarcinaeforme* and *Sclerotinia fructicola* [40-45]. The geometrical and optical isomers of 1,2-epoxypropylphosphonic acid



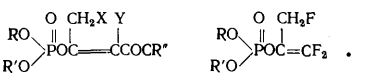
and its salts may be synthesised by the reaction of formylphosphonates and substituted ethylides [46], the thermolysis of sodium dioxolan-4-ylphosphonate [47], the reaction of α-hydroxypropionaldehyde with phosphorus tribromide followed by a rearrangement [48], by the oxidation of vinylphosphonates [49], and by other methods [44,50-53].

V. ESTERS OF TETRACOORDINATE PHOSPHORUS ACIDS

The halides of *O*-alkyl- or *O*-arylphosphoric and phosphorothioic acids are rarely used as organophosphorus pesticides in view of their low stability. However, some of them have been patented as the active principles of fungicidal preparations against *Alternaria* and *Tilletia* [35,54]:



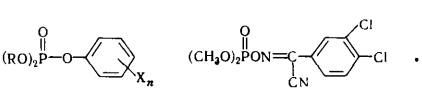
Phosphoric acid esters as a rule exhibit a moderate toxicity with respect to fungi. Among these, mention should be made of halogenovinyl phosphates obtained by the Perkow reaction from trialkyl phosphites and α-halogenocarbonyl compounds [55-57]:



Dialkyl 2-alkoxycarbonyl-1,2-dibromoalkyl phosphates can be used as soil fungicides and in the treatment of seeds to prevent root rot. They are synthesised by the addition of bromine to the double bond of the corresponding vinyl phosphates [58]:



Nitrobenzyl, pentachlorophenyl, cyanophenyl, and cyanohalogenophenyl esters of phosphoric acid (with two other alkyl groups) [59-61] and the dimethylphosphate derivative of the oxime of 3,4-dichlorophenylglyoxylonitrile [62] also exhibit a fungicidal activity:



The last preparation effectively destroys the soil fungi *Fusarium oxysporum*, *Pythium debarianum*, *Rhizoctonia solani*, and *Sclerotium rolfsii*.

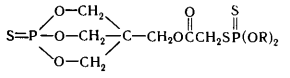
Among the esters of phosphonic and phosphinic acids, tested as fungicides, mention may be made of dialkyl 1,2-epoxyalkylphosphonates [63-65], alkyl halogenophenyl phenylphosphonates [67,69], dialkyl halogenobenzylphosphonates [68], and substituted amidines of dialkoxyphosphinyldichloroacetic acid [69]. These preparations are effective against various Gram-negative and Gram-positive microorganisms, the infection of rice by *Piricularia*, and tomato blight (due to *Phytophtora*); the majority of the preparations show little toxicity for warm-blooded animals and fish. Dialkyl sulphonylcarbamoylphosphonates are most toxic towards fungi; for example at a concentration of 0.01% diethyl toluene-*p*-sulphonylcarbamoylphosphonate suppresses the growth of more than 20 species of various phytopathogenic fungi [70,71]. Preparations of this group have been obtained by the addition of dialkyl phosphites to sulphonyl isocyanates:

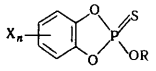


There are only isolated data about the fungicidal properties of the aryl esters of phosphorothionic and phosphonothionic acids containing various substituents in the aryl group—halogeno-, alkylthio-, alkylsulphonyl, alkylsulphonyl, trichloromethylthio-, β,β-dicyanovinyl, and certain others [72-80].

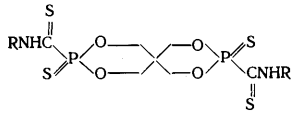
Cyclic phosphorothionates exhibit a moderate fungicidal activity in the treatment of diseases of fruit caused by

Phytophthora and *Fusarium* and of wheat smut in the *Graminae* [81-84].

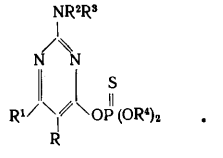




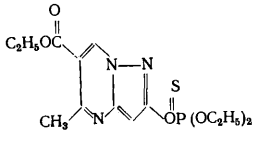
Bisthiocarbamoyl spirophosphonothioates can be used as soil fungicides and fungicides for the treatment of green plants [85]:



Phosphorothioic acid esters containing pyrimidine residues exhibit a high funcigidal activity against *Erysiphe cichoracearum* on cucumbers, *Phytophtora infestans* on tomatoes, *Puccinia recondita* and *Erysiphe graminis* on wheat, *Uncinula necator* and *Plasmopara viticola* on the vine, and *Podosphaera leucotricha* on the apple tree [86,87]:



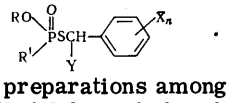
The Hechst Company has proposed a new fungicide for the treatment of the mildew of wheat and other agricultural plants—diethyl 6-ethoxycarbonyl-5-methylpyrazolopyrimidine-2-phosphorothionate (Hoe 2873) [88].



Its toxicity is 140 mg kg^{-1} for rats, 435 mg kg^{-1} for rabbits, and 184 mg kg^{-1} for guineapigs. The preparation exhibits systemic activity.

Almost all the industrial phosphorus-containing fungicides which are being manufactured in Japan belong to the group of phosphorothiolic and phosphorodithiolic acids.

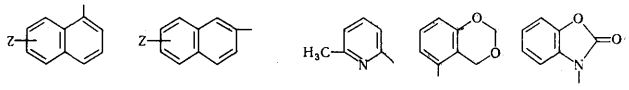
The fungicidal activity of *S*-benzyl derivatives of phosphorus acids has been investigated in detail mainly as an agent against the infection of rice by *Piricularia* [89-114]:



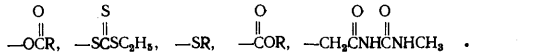
The most effective preparations among compounds of this class are *OO*-diethyl *S*-benzyl phosphorothiolate (kitazin), *OO*-di-isopropyl *S*-benzyl phosphorothioate (kitazin P), and *O*-ethyl *S*-benzyl phenylphosphonothioate (inezin).

The phosphoric, phosphorothioic, and phosphotodithioic analogues of kitazin are much less effective. The methyl and higher homologues also exhibit a lower fungicidal activity. The introduction of various substituents (alkyl, halogeno-, nitro-, methylthio-, dialkylamino-, and alkanesulphonyl) into the phenyl ring or the introduction of the COOR and CN groups in the α-position of the benzyl residue decrease the fungicidal activity of these compounds.

Kitazin analogues containing the groups indicated below in place of the phenyl ring were investigated [111-114]:



as well as analogues with various electronegative groups [115,116]:



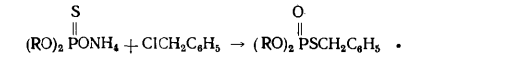
The effect of a change in the distance between the phosphorothiolic group and the phenyl ring was also studied [99]. All the preparations investigated exhibited a very moderate antipiriculariasis activity.

Kitazin, kitazin P, and inezin possess systemic fungicidal activity and are used against the diseases of rice caused by the fungi *Piricularia orizae* and *Pellicularia sasaki* at a dose of 1 kg per hectare. The toxicity of kitazin for rats is LD_{50} = 320 mg kg^{-1}, that of kitazin P is LD_{50} = 640 mg kg^{-1}, and that of inesine is LD_{50} = 750 mg kg^{-1}.

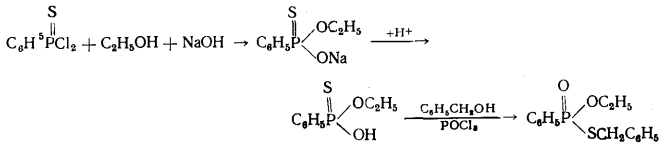
Studies on the mechanism of the action of kitazin showed that it acts on the permeability of the cell membrane of *Piricularia* fungi preventing the passage of carbohydrates and aminosugars, in particular glucose and glucosamine, into the fungal cell and promotes the loss of intracellular substances. Probably kitazin interferes with the biosynthesis of phytin in the fungal cell. It has almost no influence on the synthesis of proteins, phosphorylation processes, and endogenic and exogenic respiration [117-119].

It is noteworthy that *OO*-diethyl *S*-benzyl phosphorothioate was obtained for the first time by Kabachnik, Mastryukova, and Kurochkin in 1956 by the Michaelis–Bekker reaction [120,121]. At that time no one could even suggest that the compound might have fungicidal properties.

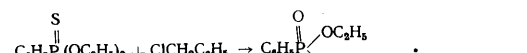
The industrial synthesis of kitazin and kitazin P consist in the benzylation of the ammonium salts of dialkyl phosphorothioates by benzyl chloride [122]:



In the manufacture of inezin, the dichloride of phenylphosphonothioic acid is treated with 3.4–3.6 moles of NaOH in 80% alcohol. The alcohol is distilled off, the residue dissolved in water, and the small amount of the *OO*-diethyl phenylphosphonothioate formed is extracted with ether. The aqueous layer is acidified and the hydrogen *O*-ethyl phenylphosphonothioate formed is esterified by benzyl alcohol in the presence of phosphoryl chloride [108,122,123]:

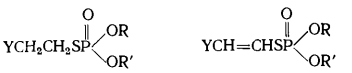


An interesting method for the preparation of inezin consists in the high-temperature *S*-benzylation of *OO*-diethyl phenylphosphonothioate by Pishchimuka's method [124]:

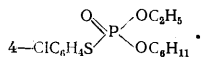


To extend the spectrum of fungicidal activity, it is suggested that mixtures of *OO*-dialkyl *S*-benzyl phosphorothioates with pentachlorobenzyl alcohol[125] or *O*-naphthyl-(*O*-aryl) *N*-methylcarbamates and also mixtures[126] of inezin with the antibiotic kasugamycin[127] be employed.

A number of studies have been made on the biological properties of β- and αβ-substituted *S*-ethyl phosphorothiolates and also *S*-vinyl phosphorothiolates:

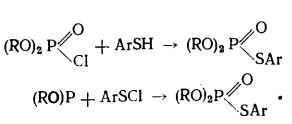


where Y = halogeno-, aryl-, alkoxy-, arylthio-, and arenesulphinyl groups and the *O*-ethyl phenylphosphorothiolate residue. All the compounds tested showed a moderate fungicidal activity in relation to *Piricularia oryzae*[128-132]. Apart from *S*-benzyl derivatives *S*-aryl esters of phosphorus acid are also effective against fungal diseases of plants[133-140]. The most active preparation in this series is *O*-cyclohexyl *O*-ethyl *S*-(4-chlorophenyl) phosphorothiolate—the active principle of cerezin. It destroys fungi of the *Corticium*, *Cochliobolus*, *Piricularia*, *Cercospora*, *Alternaria*, *Botrytis*, *Fusarium*, and *Verticillium* species:

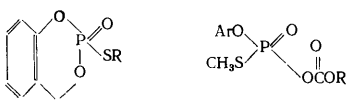


The toxicity of cerezin *per os* is 160 mg kg^{-1} for rats. *O*-Cyclohexyl *O*-ethyl *S*-(4-chlorophenyl) phosphorothiolate synergises the fungicidal activity of another preparation—hinosan. Their use in a mixture ranging from 1 : 3 to 3 : 1 makes it possible to lower the active concentrations and to improve the effectiveness of the treatment[141].

Double decomposition reactions of dialkyl phosphorochloridates (phosphonochloridates) with thiophenols or the interaction of trialkyl phosphates with arenesulphinyl chlorides have been suggested for the synthesis of *S*-aryl phosphorothiolates and phosphonothiolates[134,136-138]:



2-Alkylthio-2-hydroxy- or 2-arylthio-2-hydroxy-4-*H*-1,3,2-benzodioxaphosphorine[142-144] and the mixed anhydride of dihydrogen *S*-methyl phosphorothiolate and carbonic acid[145] have also been patented as funcigides:



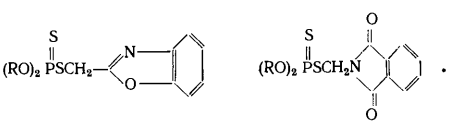
The simplest phosphorodithioates and phosphonodithioates do not exhibit a significant funcigidal activity[4]. The introduction of various electronegative substituents (halogeno-, nitro-, alkylthio-, arylthio-, alkylseleno-, trichloromethyl, alkynesulphonyl, acyl, alkoxycarbonyl, carbamoyl, and trialkylstannyloxycarbonyl groups) into the α-position of the *S*-alkyl group improves the fungidical properties of the preparations[116,146-152]. For example, *OO*-diethyl *S*-trichloromethyl phosphorodithioate at a concentration of 110 mg kg^{-1}, frees soil from infestation by *Fusarium solani*[147].

In the series of carbamoyl methyl phosphorodithioates, fungicidal activity increases on passing from *OO*-dialkyl to *O*-alkyl *O*-phenyl and further to *O*-alkyl *O*-(4-chlorophenyl) derivatives[151]:



OO-Dimethyl *S*-carbamoylmethyl phosphorodithioate forms with phenols molecular compounds the bactericidal activity of which towards *Staphylococcus aureus* and *Escherichia coli* exceeds that of the initial phenols by a factor of 10-30.[153]

Methyl phosphorodithioates containing heterocyclic residues have fairly pronounced fungicidal properties[154,155]

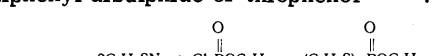


One should also note the fungicidal properties of *OO*-dialky *S*-(ω-dihalogenovinylalkyl) phosphorodithioates[156], αα-bis(dialkoxyphosphinodithioyl methyl)naphthalenes[157], 1-alkoxy-2,4-bis(dialkoxyphosphinothioylmethyl)benzenes[158], *OO*-dialkyl *S*-dialkylarsinophosphorodithioates[159], *OO*-dialkyl *S*-*O*-allylphenoxyphosphorodithioates[160], and bis(dimethoxyphosphinothioyl) sulphides and disulphides[161].

The study of the fungicidal properties of phosphorodithiolic acid derivatives led to the synthesis of the preparation quinosan—*O*-ethyl *SS*-diphenyl phosphorodithiolate[162-169]. Alkylphosphonodithiolate, phenylphosphonodithiolate, and benzylphosphonodithiolate esters have much weaker fungicidal properties[170-175]. The toxicity of hinosan for rats *per os* is LD_{50} = 150-340 mg kg^{-1}, for mice LD_{50} = 218 mg kg^{-1}, and for guineapigs and rabbits LD_{50} = 350-400 mg kg^{-1}.[176]

Hinosan is used to combat the diseases of rice caused by *Piricularia orizae*, *Pellicularia sasaki*, *Cochliobolus myiabeamus*, *Helminthosporium*, and *Hormodendrum* in doses of 0.7-1 kg of the emulsified concentrate, the treatment being repeated 2-4 times. At high concentrations the preparation is phytotoxic for the cabbage, tomatoes, and radishes[166,167]. Quinosan may be combined with cerezin (as stated above) and ethylenethiuram monosulphide as synergistic agents[176].

In the industrial synthesis of hinosan, ethyl phosphorodichloridate is treated with sodium thiophenoxide obtained from diphenyl disulphide or thiophenol[162,177]:



OS-Dialkyl *S*-phenyl phosphorodithioates are effective fungicides against the diseases of rice caused by *Piricularia*, *Helminthosporium*, and *Rhizoctonium*[178,179]. *O*-Alkyl *S*-alkyl *S*-benzyl phosphorodithiolates and *O*-alkyl *SS*-dibenzyl phosphorodithiolates have a relatively weak fungicidal activity[171,180,181].

Only a few studies have been made in recent years on the fungicidal properties of phosphorotrithioate and phosphorotetrathioate esters. *SSS*-Trialkyl, *SSS*-triaryl, and *SSS*-tribenzyl phosphorotrithioates, *SS*-diaryl chloromethyl phosphonotrithioates, and *SS*-di(alkylcarbamoylmethyl) phosphorotrithioates exhibit a moderate fungicidal activity[182-186].

The most effective preparation of this group is *O*-(2,4,5-trichlorophenyl) *SS*-di(methylcarbamoylmethyl) phosphorotrithioate, which, at a concentration of 0.003%, causes 100% suppression of the growth of the mycelia of the *Botrytis*, *Aspergillus*, *Fusarium*, and *Venturia* fungi

but it is completely non-toxic for the spores of the same fungi. It can be used against brown spot of leguminous plants and wheat grain mildew [187-190].

Products prepared by the addition of 1–8 atoms of sulphur to phosphorotetrathioates [191] and bis(dialkoxyphosphinothioyl) tri- and tetra-sulphides [192] have also been patented as fungicides.

VI. PHOSPHORUS ACID AMIDES

In the series of monoamides of phosphoric and phosphonic acids, *O*-aryl alkylphosphonamidates, phosphorylureas, and phosphorylthioureas, *OO*-dialkyl *N*-(β-aminoethyl)phosphoramidothioates, and 2-amino-2-oxo-1,3,2-benzodioxaphosphorines exhibit appreciable fungicidal activity [193-208].

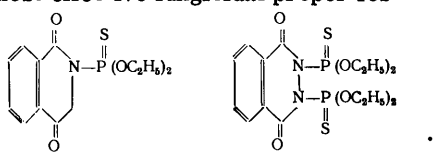
O-Pentachlorophenyl and *O*-(2,4,5-trichlorophenyl) *NN*-diethylmethylphosphonamidates suppress the growth of *Botrytis cinerea*, *Fusicladium dendriticum*, and *Fusarium oxysporum* [193]. 2,4-Dichlorophenyl derivatives exhibit a lower activity [205,206]. *OO*-Diarylphosphorylthioureas are active against *Piricularia* on rice [197-199]. *N*-Phosphorylated derivatives of 6-aminopenicillanic acid exhibit antistaphylococcal properties [201].

Phosphoramidates and phosphonamidates with alkenyl, benzyl, phosphorylalkyl and triazolyl groups attached to the oxygen or sulphur atoms as well as *N*-phosphorylated iminoesters of dihalogenocarboxylic acids proved to be weak fungicidal agents [204-208].

Among the group of amides of phosphorothiolic and phosphonothiolic acids, kitazin and inezin analogues have been patented as fungicides, but they have no advantages over their ester analogues [209-211].

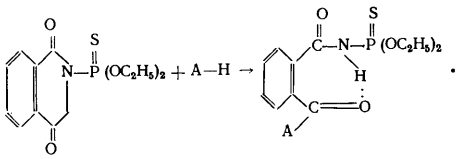
The fungicidal activity of the amides of *S*-benzyl benzylphosphonothiolic acid and ethoxycarbonyldichlorophosphoramidylmethyl disulphide and *S*-alkyl *NN*-dialkylphenylphosphonamidothiolates [212-216], which are effective against *Piricularia orizae*, *Pythium*, *Fusarium*, and *Verticillium*, is also noteworthy.

Among the large number of compounds which Tolkmith synthesised and tested in the study of *N*-acylated and *NN*-diacylated phosphoramidothioates, *OO*-diethyl phthalimidophosphonothioate (Dowco 199 preparation) and *NN'*-bis(diethoxyphosphinothioyl)benzopyridazinedione exhibit the most effective fungicidal properties [217-226]:



The Dowco 199 preparation is used against apple scab, powdery mildew of cucumbers, *Sphaerothaeca* on rose bushes, and certain other diseases at a concentration of 0.015–0.06%. The preparation is highly toxic for warm-blooded animals (5000–5500 mg kg^{-1}).

In order to explain the mechanism of the fungicidal activity of *OO*-diethyl phthalimidophosphonothioate, Tolkmith suggests that it acylates amidases interfering thereby with vital metabolic processes in the fungal cell:

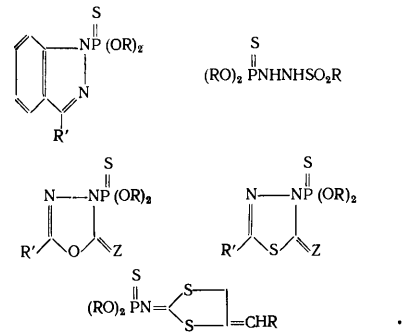


The high activating capacity of the Dowco 199 preparation accounts for its low anticholinesterase activity.

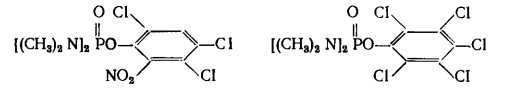
Several methods have been described for the synthesis of *OO*-diethyl phthalimidophosphonothioate: by the interaction of phthaloyl chloride with *OO*-diethyl phosphoramidothioate and triethylamine, by treating potassium phthalimide with *OO*-diethyl phosphorochloridothioate, and by the reaction of phthalic anhydride with the *OO*-diethyl phosphoramidothioate anion obtained from the corresponding amide and sodium hydride in dimethylformamide [219,221,225].

In the study of the effect of the chemical structure of chemical analogues of the Dowco 199 preparation on their biological activity, it was shown that the introduction of substituents into the phenyl ring and its hydrogenation decrease the fungicidal activity by a factor of 10–20.

In the series of phosphonamidothionates and phosphonothionates, *OO*-diethyl indazolylphosphonothioates [227,228], *N*-(*OO*-diethylphosphorothioyl)-*N'*-sulphonylhydrazines [229], *N*-(*OO*-dialkylphosphorothioyl)oxadiazines and *N*-(*OO*-dialkylphosphorothioyl)thiadiazines [230], and 4-alkylene-2-(*OO*-dialkylphosphorothioylimino)-1,3-dithiolanes [231] also possess fungicidal properties:

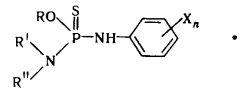


Among phosphoric acid diamides, *O*-aryl *NNNN'*-tetramethylphosphorodiamidates containing electronegative atoms and groups in the aryl substituent exhibit a high fungicidal activity [232-237]:



The above two preparations are now being tested as experimental fungicides. The first was developed in the Czechoslovak Socialist Republic. Its toxicity for warm-blooded animals is 10 mg kg^{-1} when introduced to rats via the stomach. The second preparation was patented as early as 1962 (Schoot et al. [236]), but its field tests were reported only at the Fifth British Conference on Insecticides and Fungicides [237]. The preparations are effective against the fungi (*Erysiphe graminis* and *Erysiphe cichoracearum*) responsible for the powdery mildew on barley and cucumbers.

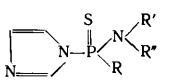
Mel'nikov and Vladimirova made a systematic study of the fungicidal activity of *N*-arylphosphorodiamidothioate esters [238,239]:



The introduction of the methyl group and of chlorine atoms in the aryl substituent increases the fungicidal activity of the preparation; alkyl esters are more active than aryl esters and *N*-alkylamido-derivatives are more effective than the dialkylamido-derivatives. *O*-Ethyl *N*-(4-chlorophenyl-*N*-methylphosphoramidothioate yielded satisfactory

results against the *Peronospora* infection of tobacco and the wilting of fodder beans caused by *Fusarium*[238].

Imidazolylphosphoramidothioates and imidazolylphosphonamidothioates possess a high fungicidal activity[220,230-246]:



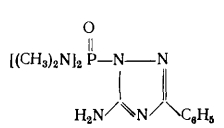
In a study of the biological activity of this group of preparations against the powder mildew of cucumbers and the potato disease caused by *Phytophtora*, it was shown that in such cases the fungicidal activity of the compounds is maximal when R is a planar substituent, for example phenyl. Derivatives of dihydrogen *O*-ethyl and dihydrogen *O*-aryl phosphorothioates and also of cyclohexylphosphonothioic acid are less effective[220,246]. The influence of the polarity and steric properties of the substituent at the phosphorus atom on the fungicidal activity of imidazolylphosphoramidothioates is more complicated than for cholinergic preparations.

It is interesting to note that the toxicity of the optical isomers of *NN*-diethylaminophenyl imidazolylphosphonothioate for *Phytophtora infestans* is independent of the sign of the optical rotation of the isomer, while the toxicity of the (−)-isomer for white mice is twice as high as that of the (+)-isomer (147 and 316 mg kg^{-1} respectively)[241]. Probably the mechanism of the fungicidal activity is related to the dissociation of the P–N bond, the elimination of the imidazole residue, and its inclusion in the metabolic processes of the fungus[244].

2-Aryloxy-2-thionobenzo-1,2,3-diazaphospholens, *O*-aryl *N*-acylphosphorodiamidothioates[247], *S*-benzyl phosphorodiamidothioates[248], 3-[*O*-alkyl-*N*-alkylphosphoramidothioyl]-5-alkoxy-1,3,4-thiadiazol-5-ones[249], and 1-(*O*-alkyl-*NN*-dialkylphosphoramidothioyl)imidazolidine-2-thiones[250] have also been proposed as fungicides.

There are only isolated data about the fungicidal activity of phosphorodiamidodithioic acid. *NNNN'*-Tetraalkyl-*S*-thiocarbamoylphosphorodiamidodithioates[251] and 2-anilino-2-thiono-3-phenyl-4,5-benzo-1,3,2-thia-aza-phosphorin-6-one possess fungicidal properties[252].

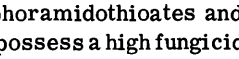
The study of the fungicidal activity of phosphorus acid triamides is associated mainly with the work of van den Bos on the *N*-phosphorylation of nitrogen-containing heterocycles by phosphorodiamidochloridates and phosphorothioates. Among this group of compounds, the preparation "Wepsyn", 2-amino-4-phenyl-1,3,5-triazolylphosphonic acid *NNNN'*-tetramethyldiamide, is used on a small scale against the fungi responsible for the powder mildew on decorative and fruit-bearing cultivated plants. The preparation is active both on spraying the leaves and when administered through the roots. It exhibits a systemic activity. Wepsyn makes the plants resistant or, in other words, it stimulates the synthesis of phytoalexins[253,254]:



Some of the Wepsyn analogues are effective against *Erysiphe cichoracearum* on cucumbers and *Erysiphe graminis* on barley and oats[255].

In order to enhance their fungicidal activity and decrease their phytotoxicity, imidazolylphosphonodiamidothioates can be used as complexes with calcium, cobalt, copper, iron, manganese, nickel, and zinc salts[256].

The fungicidal properties of phosphorodiamidoyl- and phosphorothioyl-sulphonylhydrazides are also noteworthy[257]:



Among other classes of organic phosphorus compounds, tetra-arylalkylenebisphosphine oxides[258], triphenylphosphinomethylenes[259], di-iodotriphenylphosphorane[260], arenesulphonylphosphazo-compounds[262], derivatives of cyclotriphosphazine[262], and 5-alkyl-1,1,3,3-tetraphenyl-1,3-diphospha-5-bora-2,4,6-triazines[263] have been patented as fungicides.

The review has shown that intensive studies on the fungicidal properties of organophosphorus compounds are being made in different countries. One of the useful properties of phosphorus compounds is their relatively low stability and rapid metabolic breakdown in plants, in animal organisms, in soil, and other components of the environment with formation of products which are safe for man and domestic animals. Another important feature of these compounds is the high selectivity of their action.

Phosphorus-containing fungicides act on metabolic processes within the fungal cell, on the permeability of the cell membrane, as well as on the inter-relation between the host plant and the parasitic fungus.

For a specific synthesis of new fungicidal preparations, it is necessary to extend biochemical research on the mechanism of the action of phosphorus-containing fungicides on the fungal cell.

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Polarography in Organic Media

S.I.Zhdanov

Brief consideration is given to fundamental aspects—the technique of a polarographic experiment in an organic medium, factors producing a change in polarographic behaviour when water is replaced by an organic solvent, and specific features of the polarographic behaviour of inorganic and organic depolarisers—and a list of 42 references is included.

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1. INTRODUCTION

Polarography was discovered in 1922 by the well known Czechoslovak Nobel prizewinner J. Heyrovský during the investigation of aqueous solutions. This method yielded much valuable information on the mechanism and the kinetics of electrode processes in aqueous media. But soon after the discovery it became necessary to use the method also to investigate solutions in mixtures of water with organic solvents and in pure organic solvents. The original reason was the limited solubility in water of many organic and inorganic substances (e.g. elementary sulphur), whose polarographic behaviour was of interest. At the present time, however, the use of organic solvents in polarography is dictated also by the valuable information on the mechanism and kinetics of electrode processes and on the properties of solutions obtainable by working with organic solvents. The elucidation of the mechanism of the electrochemical reduction and oxidation of many classes of organic compounds, the generation and investigation of the radical-ions of organic and inorganic substances (oxygen, sulphur), the establishment of the differentiating action of organic solvents for strong inorganic acids, and other surprising results obtained with organic solvents struck the imagination and initiated a powerful new stream of investigations on these lines. It is therefore of interest to examine some fundamental aspects of the use of organic solvents in polarography. More detailed, specific information will be found in numerous reviews and also in a monograph [1].

2. EXPERIMENTAL TECHNIQUE

The development of polarography in organic media has been stimulated by advances in the chemistry and electrochemistry of organic solvents and solutions in them [2-5], by the preparation of new organic solvents having very interesting properties (propylene carbonate, an aprotic solvent having a high dielectric constant; hexametapol, in which solvated electrons exist for quite a long time; etc.), and by the production of new polarographic apparatus, especially potentiostatic instruments, which enable perfectly satisfactory polarograms to be recorded with poorly conducting solutions.

Considerable experience has accumulated of working with organic solvents. The purity of the supporting electrolyte is of primary importance for polarography in organic media. In practice it must be freed mainly from contamination with electrochemically active substances (depolarisers) and proton-donors, in particular water, if the experiment is to be conducted under aprotic conditions. On storage the purified solvents again accumulate undesirable impurities as a result of their hygroscopicity and decomposition. It is therefore advisable to work with freshly purified solvents. In some solvents peroxy-compounds, which give sharp reduction waves, appear on storage. Oxolan, for example, is best freed from peroxides by being boiled with potassium permanganate [6].

Oxygen is usually more soluble in organic solvents than in water, and is more difficult to displace from organic media than from aqueous solutions. The rate of expulsion of dissolved oxygen is increased by passing fine bubbles of an inert gas through the solution; this is achieved by inserting porous glass plates at the gas inlet into the cell. Nitrogen and electrolytic hydrogen from cylinders must be freed from traces of oxygen by combustion over catalysts or adsorption on metallic copper or other adsorbent. It is considerably more convenient to use argon, which requires no further purification, since its oxygen content lies within permissible limits. Sulphate is not employed to remove oxygen from solutions in organic solvents, since either it is sparingly soluble or it reacts slowly with oxygen.

The solvents are rigorously dried by means of powerful drying agents—alkali metals, molecular sieves, electrolysis, etc.—followed by fractionation under reduced pressure and in an inert atmosphere to avoid decomposition and oxidation, especially with high-boiling solvents.

Water of crystallisation in a salt used to prepare the supporting electrolyte or as depolariser may seriously moisten the electrolyte and nullify all efforts to dry the solvent. The salt must therefore be dried no less thoroughly. It is very difficult to remove the last traces of moisture from salts. The latter must be heated in the presence of strong drying agents in a vacuum for a long time or else melted preferably in a vacuum. But not all salts are completely freed from moisture by vacuum melting (lithium perchlorate, for example, still contains 0.1% of water [7]). Where maximum dryness is required

during an experiment, therefore, it is useful to treat the final electrolyte with such drying agents as molecular sieves or alkali metals. Salts of strongly hydrolysed multivalent metals (titanium, zirconium, hafnium, thorium, aluminium, etc.) are difficult to dry, since they decompose on dehydration of the crystalline hydrates, with formation of sparingly soluble oxy-salts. In such cases either the behaviour of the hydrates is studied [8] or the anhydrous salts are prepared under conditions excluding access of moisture.

The dehydrated solvents and solutions rapidly absorb moisture from the surroundings. It is therefore best to conduct all operations with them in an atmosphere of a dry inert gas in hermetically sealed boxes.

The water content of solvents and solutions is most often determined by titration with the Karl Fischer reagent. The Reviewer's experience has shown that water can be determined considerably less laboriously and no less accurately from the volume of hydrogen evolved on contact of a portion of the solution with calcium hydride [9]. A very sensitive ($\ll 0.01\%$) method proposed [10] for the determination of water is based on its reaction with lead tetra-acetate, the precipitated lead dioxide being estimated spectrophotometrically. Pure calcium carbide is required for the determination of small concentrations of water by gas–liquid chromatography.

The above procedures enable solutions to be prepared whose water content can be lowered to 10^{-4} M or below. In most cases, of course, such rigorous drying of the solutions is not required, since even large quantities of water by no means always effect the polarograms. The radical-anion of piazthiole, for example, is protonated by water so slowly that, in admixture with dimethylformamide, the first reduction wave of piazothiole to the radical-anion still remains completely unchanged even with water contents up to 40 vol.%, [11] and this case is by no means exceptional. The insensitivity of many electrode processes to traces of moisture enables us to work with organic solvents under ordinary laboratory conditions. Since many methods of pretreating solvent, salts, and solutions are laborious, they must be applied only where necessary.

Quite often, however, the whole arsenal of means must be used for removing moisture from the solutions. If the depolariser reacts with water, the presence of traces of moisture will lower its concentration and produce other complications. Dessy et al. [12] pointed out the need for careful drying of aprotic solutions for this reason in the investigation of organometallic compounds. Experimental conditions of maximum dryness are extremely desirable also because they may lead to the detection of radical species and also unusual valency states of elements that are otherwise too unstable.

In the choice of salt for the preparation of supporting electrolytes it is quite insufficient to assess solubility from the dielectric constant ϵ of the solvent. Experience shows that solubility and solvation often depend not only on the polarity of the solvent molecules but also on specific interaction of the ions with the solvent. The relatively non-polar pyridine ($\epsilon = 12.5$), for example, is a fairly good solvent for ionic salts, whereas formamide ($\epsilon = 113$) is comparable only with pyridine in solvent power, but is inferior to water [8].

Cations are solvated by coordination with electron-donor solvent molecules (whence the high solubility of salts in pyridine), whereas anions, which themselves are electron-donors, may be solvated by electron-acceptor solvent molecules or by hydrogen-bonding. Since hydrogen bonds are weaker than bonds in the solvates of cations, the nature of the anion strongly influences the solubility of the salt as a whole. The solubility of halides falls on passing from iodides to chlorides, while fluorides are usually sparingly soluble. Perchlorates, nitrates, nitrites, and thiocyanates are more soluble, whereas sulphates, carbonates, phosphates, oxides, and sulphides are in general insoluble [8].

Lithium perchlorate and chloride as well as tetra-alkylammonium iodides and perchlorates, which are very soluble, are most often used as supporting electrolytes in organic solvents. The maximum potential range within which mercury is polarised ideally (the polarographic range) is provided by a tetra-alkylammonium perchlorate. Thus with tetraethylammonium perchlorate in dimethylformamide we can work at potentials from +0.45 to −2.8 V relative to the saturated calomel electrode (s.c.e.). [8] This supporting electrolyte is interesting also because it exhibits the least tendency to form ion-pairs with radical-ion products of electrode reactions.

The electrical conductivities of the best electrolytes in organic solvents are considerably inferior to those of aqueous solutions. An optimum salt concentration, ensuring maximum conductivity of the solution, exists for most solvent–salt pairs. This concentration is usually close to molar, which it is desirable to ensure. With a solvent of low ionising strength, nevertheless, even fairly concentrated salt solutions are comparatively poor conductors, since a considerable proportion of the ions are combined as ion-pairs, and are not involved in the transport of current through the electrolytes. For this reason it is difficult to work with anhydrous solvents such as oxolan and dioxan.

It is often necessary to correct the polarograms for the voltage drop iR in the solution. This is best done by calculating the resistance R of the cell at the required instant t in the life of the drop from the resistivity ρ of the electrolyte [13]:

$$R = \frac{0.191\rho}{m^{1/3}t^{1/6}} \qquad (1)$$

where m (g s^{-1}) is the rate of efflux of mercury from the capillary. A reversibly dischargeable pilot ion, whose half-wave potential $E_{\frac{1}{2}}$ is independent of its concentration, can be used [14]. Inclusion of a Luggin–Haber capillary in a potentiometric cell, e.g. in work with a potentiostatic polarograph, can eliminate only part of the voltage drop, since the latter is largely concentrated near the mercury drop [13]. Rather better elimination can be achieved by arranging auxiliary, indicator, and standard electrodes in that order in a straight line.

Potentiostatic polarographs completely eliminate the effect of instability of the potential of the mercury floor as auxiliary electrode, which is especially marked in the presence of perchlorates. When polarograms are recorded by means of the usual polarograph, the potential of the indicator electrode relative to a reliable reference electrode must be measured periodically, and the polarogram must then be replotted on a linear potential scale, in order to avoid stretching of the waves and the appearance of spurious inflections, falls in current, and hysteresis phenomena.

Various electrodes of the first or second kind are used as reference electrodes, either in the test solution or externally. Very often an external aqueous calomel electrode is employed. A diffusion potential of unknown magnitude appears at the junction between aqueous and non-aqueous solutions. This is of no importance when the behaviour of different compounds in the same solvent is

compared, but it prevents a quantitative comparison of the behaviour of a given depolariser in different solvents. In this connection an electrode of the second kind may be useful, e.g. a silver chloride electrode placed in a saturated solution of a salt having a common anion (chloride). The potential of such an electrode will be independent of the composition of the medium, since the activity of the potential-determining ion will remain constant [15,16].

Several redox systems having large, weakly solvated, univalent cations, whose potentials can be regarded to a first approximation as independent of the nature of the solvent, have also been proposed for this purpose. On Pleskov's suggestion [17] the potential of the Rb/Rb^+ electrode is taken as standard, but Strehlow introduced the ferrocene–ferricinium and cobaltocene–cobalticinium systems [3,18], of which the former has become more widely used. It must be borne in mind, however, that the potential of such an electrode is only approximately independent of the nature of the solvent. The use of such systems to reveal fine effects is therefore inadmissible. In aqueous–alcoholic solutions, for example, the limiting current of the ferricinium ion changes not only with the viscosity η of the medium but also with the degree of solvation [19].

By means of such standard systems it has been established that the liquid junction potential between an aqueous saturated calomel electrode and acetonitrile, propionitrile, isobutyronitrile, phenylacetonitrile, and acetone is 0.25 V, which must simply be subtracted from the potential measured in the organic solvent relative to the aqueous reference electrode [20].

One of the most important properties of an organic solvent for polarography is its proton-donor activity. On this principle solvents can be classified as protic, aprotic, and non-protic [21]. Solvents which are proton-donors can be divided into three groups: (i) hydroxylated solvents include water, alcohols, glycols, and phenols; (ii) protogenic solvents are considerably stronger acids than water; and (iii) protophilic solvents are considerably stronger bases than water. Aprotic solvents possess neither acidic nor basic properties by definition, but in fact, with the exception of pyridine and similar compounds, they (dimethylformamide, dimethyl sulphoxide, acetonitrile, oxolan, etc.) exhibit nevertheless weak acidic or basic properties. For example, dimethyl sulphoxide is a considerably weaker acid than water, but is comparable with it in basic strength. Finally, non-protic solvents contain no hydrogen at all in their structure (sulphur dioxide, carbon tetrachloride) and cannot act as Brønsted acids, but exhibit Lewis acid–base properties.

3. CAUSES OF CHANGE IN BEHAVIOUR OF DEPOLARISERS ON PASSING FROM AQUEOUS TO ORGANIC MEDIA

Several factors influence the change in polarographic behaviour on passing from aqueous solutions to solutions in organic solvents.

1. Since the mercury-solution interfacial tension depends on the composition of the latter, change of solvent affects the drop time τ of the electrode. The effect of τ on the limiting diffusion current i_d is fully represented by the Ilkovič equation and its modifications. The change in τ may have some effect on the half-wave potentials of irreversible waves.

2. The viscosity of the medium changes on passing to another solvent, and this entails a change in diffusion coefficients. It is easy to show by means of the Ilkovič equation and the Stokes–Einstein equation ($D = kT/6\pi\eta r$) that

$$i_d \eta^{1/2} r^{1/2} = \text{const}. \qquad (2)$$

Systematic data on the effect of solvent composition on the limiting diffusion current through variation in diffusion coefficient will be found in Schwabe's publications [22–24]. Change in diffusion current is usually produced by changes not only in viscosity but also in solvation of the depolariser particles r.

3. Replacement of the solvent affects the acid–base and other equilibria in the solution (solvation, association, complex formation). This effect has many important consequences.

(*a*) Acids and acidic components of buffer mixtures are usually weaker in organic solvents, and the pH is higher. The half-wave potential of a reversible reduction wave involving ν hydrogen ions and n electrons becomes more negative [22–24]:

$$\partial E_{1/2}/\partial \mathrm{pH} = -59.1 \frac{n}{\nu}. \qquad (3)$$

(*b*) If the depolariser becomes less strongly solvated, the reversible reduction wave undergoes a positive shift, whereas weakening solvation of the product produces a shift in the opposite direction along the potential axis. The energy of interaction with the solvent depends on the dielectric constant ϵ of the medium and the particle size r. From the Born equation the standard reversible discharge potential of cations can be written [25]

$$E_0 \simeq E_{1/2} \simeq A + eZ/2r\epsilon. \qquad (4)$$

If r is assumed to be independent of the composition of the medium, i.e. if we neglect the role of specific interaction between cation and solvent, it follows from Eqn. (4) that the half-wave potential should become less negative with decrease in dielectric constant, while the product $E\frac{1}{2}\epsilon$ remains constant. In practice, however, this product is rarely constant: strictly speaking, the product $E\frac{1}{2}\epsilon r$ should be constant. Weakening solvation of the depolariser diminishes the degree of irreversibility: processes quite often occur reversibly in organic solvents that are completely irreversible in aqueous solutions [8].

(*c*) Ionic interactions are strengthened by weakening solvation of the cations of the supporting electrolyte. Much experimental information has accumulated on the effect of the nature and concentration of these cations on the reduction waves of aromatic hydrocarbons in aprotic solvents, which is governed by the formation of ion-pairs with radical-anions and dianions of the hydrocarbons [26–30]. The formation of ion-pairs displaces the waves to less negative potentials. The effect is greater the higher the charge on the hydrocarbon anion ($R^{\cdot-}$ or R^{2-}) and the cation of the supporting electrolyte, the smaller the crystallographic radius of the cation, and the higher its concentration. It is supposed that the radical-ions do not interact with tetra-alkylammonium cations; dianions interact most strongly with lithium ions. Multiply charged cations produce a very large displacement of the waves even at low concentrations: thus 0.002 M $Nb(ClO_4)_3$ displaces the half-wave potentials of the first and second waves in 0.003 M quinone in acetonitrile by 550 and 950 mV respectively [28]! Both this phenomenon and solvation are analogous to complex formation, and the composition p of the ion-pair and its equilibrium formation constant K_{eq} can be calculated from the displacement

of the half-wave potential by means of the equation[28]

$$(E_{1/2})_{cat} - (E_{1/2})_0 = \frac{RT}{F} \ln K_{eq} + \frac{RT}{F} p \ln [M^+] \quad . \qquad (5)$$

For example, the radical-anion of anthraquinone forms a 1 : 1 complex with lithium ion in dimethylformamide, having Keq = 39 M^{-1}, whereas the dianion associates with three lithium ions[28].

4. Adsorption of the solvent on the mercury may retard tangential movement of the electrode surface, and thus eliminate polarographic maxima, which are suppressed e.g. by aliphatic alcohols[22,31]. Adsorption of the solvent can in principle inhibit electron transfer.

5. An organic solvent diminishes the adsorbability of other substances, primarily organic, and is thereby able to produce various effects.

(*a*) Surface-active substances, which suppress polarographic maxima in aqueous solutions, are largely ineffective in organic solvents. In order to eliminate tangential movement in the latter, therefore, use must be made of such strong surface-active agents as dodecyl sulphate, dodecylamine hydrochloride, dodecylammonium dodecyl sulphate, octadecyl sulphopropionate, etc.[8]

(*b*) Weakening of the adsorption of depolariser and reaction product in reversible systems leads to the disappearance of adsorption waves preceding and following Brdička waves.

(*c*) With self-inhibition due to the adsorption of depolariser or reaction product, the weakening of adsorption in organic solvents leads to an increase in current, i.e. to elimination of the self-inhibition effect[32].

(*d*) Weakening of adsorption of the depolariser produces a cathodic shift in irreversible reduction waves[22-25,33].

(*e*) Kinetic and catalytic surface waves undergo greater changes in organic solvents also because of decrease in the surface concentration[33].

(*f*) In several cases the decrease in adsorbability changes the mechanism of the process. Stradyn' and Kravis have shown that, in alkaline aqueous–ethanolic solution, the first four-electron wave of nitrobenzenes separates into one- and three-electron waves. The splitting of the wave is caused by insufficiently rapid protonation of radical-anions in the surface layer of solution owing to their desorption[34].

(*g*) Elimination of adsorption phenomena by organic solvents improves the correlation between half-wave potentials and substituent constants, and permits more accurate establishment of the composition and stability of complexes with ligands that from aqueous solutions are adsorbed on mercury.

6. Organic solvents influence the structure of the electrical double layer. This undoubtedly affects the kinetics of electrode processes involving slow discharge.

4. INORGANIC DEPOLARISERS

In many organic solvents alkali-metal ions are reduced reversibly. Only the lithium ion, the most strongly solvated, exhibits some irreversibility[35]. Most bivalent cations are Lewis acids, and can be solvated by a basic solvent. In aprotic solvents they are more weakly solvated than in water, and are reduced more easily[20].

Readily hydrolysed multiply charged ions (Ti^{4+}, Th^{4+}) are reduced considerably more easily in acetonitrile than in water. Whereas in aqueous solutions the waves are attributed to the discharge of water molecules constituting the hydrate sheaths of ions, with the evolution of hydrogen, in acetonitrile thorium, for example, forms an amalgam, though not in high yield[8].

Many anions are stabilised in protic solvents by hydrogen bonds. This possibility does not arise in aprotic solvents. Therefore the activity of anions is higher in such solvents than e.g. in water. Anions may be stabilised in aprotic solvents by interaction with a Brønsted acid (HX^{2-}) or with a Lewis acid, i.e. with cations. The stability of anion–cation complexes is considerably greater in aprotic solvents than in water. This is evident from the cathodic shift in the anodic dissolution potential of mercury. Thus on passing from water to acetonitrile with an anion concentration of 0.001 M this potential shifts from 0 to −1.16 V in the presence of the hydroxide ion, from −0.1 to −0.71 V in the presence of the iodide ion, and from +0.1 to −0.61 V in the presence of the chloride ion[20].

An especially interesting result was obtained for the reduction of oxygen in aprotic solvents. Polarography cyclic volt–ammetry, and electron spin resonance established that in dimethyl sulphoxide the first stage consists in transfer of a single electron to the oxygen molecule with formation of a superoxide radical-anion $O_2^{\cdot-}$. This highly reactive species is quite stable in aprotic solvents. It is curious that the electron is transferred almost reversibly under these conditions, whereas in aqueous solutions transfer of the first electron is assumed to be the limiting stage[36].

On platinum, graphite, and gold electrodes in dimethyl sulphoxide, oxolan, and dimethylformamide elementary sulphur S_8 also undergoes one-electron reduction with formation of the radical-ionic species $S_8^{\cdot-}$, which is stable for several days[37]. Sulphur reacts with mercury to form mercury sulphide. The mechanism of the reduction of sulphur is therefore different at a dropping mercury electrode.

It is remarkable that strong mineral acids are differentiated in solvents, such as acetonitrile, that are weaker bases than water and dimethyl sulphoxide. Perchloric, sulphuric, and hydrochloric acids give identical hydrogen-evolution waves in water, but separate waves in acetonitrile, and can be determined when present together[20,21]. A linear relation exists between the pKa value of the acid in water (with p$K < 3$) and the half-wave potential of hydrogen evolution in pyridine[38].

The use of organic solvents in polarography shows promise for the analysis of metals after extraction by organic solvents without a re-extraction stage.

5. ORGANIC DEPOLARISERS

The use of aprotic organic solvents in the polarography of organic compounds has led to fundamental changes in our views on the mechanism and the kinetics of electrode processes involving them. It had previously been assumed, when many-electron and completely irreversible waves were observed in aqueous and waterlike solvents, that the limiting stage was slow transfer of the first electron. The use of aprotic solvents enabled these many-electron processes to be separated into individual elementary stages. Alternating-current polarography and cyclic volt-ammetry showed that the first electron is transferred immeasurably rapidly in organic electrochemistry, but transfer of the second electron is sometimes slow[39,40]. The irreversibility of processes in protic solvents is due to secondary chemical reactions,

mainly protonation of radical-anions and dianions. One of the few exceptions to date is the reduction of halogeno-derivatives, which is irreversible also in aprotic solvents. However, the probable cause of irreversibility even in this case is rupture of a carbon–halogen bond after or during transfer of the first electron, not slowness of the actual electron-transfer stage.

In conclusion we note that maximum accuracy of correlation of half-wave potentials with substituent constants may be ensured by the use of aprotic solvents and supporting electrolytes with cations of large radius, since only under such conditions does the half-wave potential best represent the electron affinity of the molecule. In protic solvents such correlations are complicated by preceding and following chemical reactions, as well as by simultaneous transfer of more than one electron [41,42].

It follows also from the above account that the use of aprotic solvents in a.c. polarography opens up great new possibilities for highly sensitive analysis of inorganic and organic compounds, since in many cases processes take place reversibly under these conditions.

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Institute of Electrochemistry,
USSR Academy of Sciences,
Moscow

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Physicochemical Foundations of Micellar Catalysis

I.V.Berezin, K.Martinek, and A.K.Yatsimirskii

The structure and the properties of micelles of surface-active substances in aqueous solution are briefly surveyed. Attention is paid mainly to solubilisation and methods for investigating the location of solubilised molecules. Kinetic concepts of micellar catalysis are examined and compared. The role of various factors (concentration effect, orientation, shift in pK_a of reactants, change of environment) in the micellar effects observed in organic reactions is analysed. A list of 113 references is included.

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I. INTRODUCTION

Research on the effect of surface-active agents on the kinetics of organic reactions in aqueous solution has recently become a separate branch of physical organic chemistry. Interest in this problem has arisen mainly from the fresh opportunities both for controlling the rates of chemical reactions and for studying their mechanism[1,2].

The presence of a surface-active agent usually produces a 10–100-fold acceleration or deceleration of the reaction; in individual cases reaction velocities are increased by factors of 10^3–10^4.[1-4] It has now been finally established that these effects are due to the presence not of individual molecules but of association complexes (micelles) containing a large number of molecules of the surface-active agent. This fact has been responsible for the appearance of the term "micellar catalysis".

Micellar catalysis is also of interest to biochemists, for several aspects of this phenomenon exhibit features recalling the mechanism of the action of enzymes[5-8].

Surface-active agents may also be used in organic syntheses[1,2], e.g. in reactions between water-insoluble substances in aqueous solution (the most important application of this is emulsion polymerisation[9,10]).

Micellar catalysis may also be assumed to play some part in the bactericidal action of surface-active agents mixed with other bactericidal preparations. An example is the dependence of the time of destruction of *Bacillus coli* bacteria by a solution of phenol (0.54%) on the concentration of a dialkyl sulphosuccinate anionic surface-active agent (Aerosol MA).[11] The efficiency of the phenol is greatly increased by the formation of micelles in the solution of the surface-active agent (when the critical micelle concentration (c.m.c.) is reached), after which it passes through an optimum. As will be shown subsequently, both these features are characteristic of micellar catalysis.

The number of papers on the kinetics of chemical reactions in the presence of micelles of surface-active compounds began to increase sharply after 1960, and now exceeds fifty (excluding papers on emulsion polymerisation). An exhaustive survey of work on micellar catalysis

(up to 1970) was made by E. and J. Fendler[2], who reviewed systematically all available published information on the mechanisms of the catalysed reactions. The present paper attempts to discuss the physicochemical basis of micellar catalysis†. Attention will be paid mainly to explaining the kinetics of chemical reactions occurring in the presence of the micelles of surface-active compounds and to establishing the rôle of the principal factors—the close approach (concentration) of reactants attached to the micelle, their mutual orientation, the change in the environment, and with ionic micelles the effect of the micellar charge on the transition state in the reaction—causing the change in reaction velocity in the presence of micelles. An analysis of these factors must take into account the structure of the micelles and the laws governing their formation and interaction with other solutes. The first part of the Review will therefore report the necessary information on the physicochemical properties of aqueous solutions of surface-active agents.

II. PHYSICOCHEMICAL PROPERTIES OF AQUEOUS SOLUTIONS OF SURFACE-ACTIVE AGENTS

Among the many aspects connected with the problem of the physicochemical properties of aqueous solutions of surface-active agents[12-15] we shall consider only those which are directly related to micellar effects in the kinetics of chemical reactions.

1. Formation and Structure of Micelles in Aqueous Solutions of Surface-active Agents

Surfactant molecules possess well defined diphilic properties: i.e. they contain both hydrophobic and hydrophilic groups. They usually have the structure RX, where R is a hydrocarbon chain containing 8–18 carbon atoms, an alkylaromatic radical, or other type of hydrophobic residue, and X is a hydrophilic group. Depending on the nature of X surface-active agents can be divided into non-ionic, anion-active, and cation-active. In the last case the hydrophilic residue is usually a quaternary ammonium, pyridinium, or phosphonium group; the anion-active compounds contain a sulphate, sulphonate, phosphate, or carboxylate group; in non-ionic surfactants X represents a polyoxyethylene residue. Zwitterionic surface-active compounds constitute a special class[13].

Surface-active substances are characterised by several specific features—(i) the ability to lower the surface tension in solutions by adsorption and orientation at interfaces, (ii) very low maximum concentration of the molecular form in solution, (iii) formation of micelles above a certain concentration (critical micelle concentration, c.m.c.), and (iv) ability to solubilise water-insoluble substances within and on the surface of the micelles—all of which are closely interrelated[12,14]. The last two properties are of interest in connection with micellar catalysis, and will be considered in greater detail below.

In fact the formation of micelles takes place in a narrow range of surfactant concentrations around the c.m.c. and is accompanied by a sharp change in several properties of the solution (light scattering, viscosity, electrical conductivity, surface tension, solvent power for certain substances, etc.), which is used for determining the c.m.c. The "experimental" value of the c.m.c. may depend significantly on the property and on the method of measurement; when a third component (e.g. a dye) is used, its presence may cause a shift in the c.m.c. [16]

Theoretical statistical-mechanical models of micelle formation[17,18] are by no means perfect, and merely enable the presence of a minimum in the dependence of the free energy of the system on the aggregation number to be established. Nevertheless, the rôle of several factors which lead to micelle formation can be traced on the basis of these models. The main driving force causing the association of surfactant molecules is the hydrophobic interaction of their hydrocarbon chains.

The following generalisations apply to micelle formation. The shorter the hydrocarbon chain the smaller the decrease in free energy of the system resulting from aggregation and the higher the concentration at which the surfactant molecules have the same chemical potential in the dissolved state and in the micelle, and hence the higher the critical micelle concentration. Factors that diminish the electrostatic repulsion of the hydrophilic groups favour micelle formation. Thus increase in the concentration of gegenions considerably lowers the c.m.c. of ionic surfactants. With the non-ionic compounds micelle formation is promoted by rise in temperature, which diminishes the hydration of their hydrophilic groups. Higher alcohols also lower the surface charge density on an ionic micelle and diminish the c.m.c. On the other hand, methanol and similar compounds (dioxan, ethylene glycol), which do not penetrate a micelle to the same extent, have a weak effect on the c.m.c., raising it in high concentrations by decreasing the energy of hydrophobic interaction between the hydrocarbon chains of the surfactant molecules.

Enlargement of the micellar aggregates, i.e. separation of the surfactant as a macrophase, is prevented by hydration of the hydrophilic group, steric factors, entropy losses, and electrostatic repulsion of head groups in the case of ionic surfactants. In terms of the general theory of the thermodynamic stability of two-phase disperse systems the stability of micelles is probably determined by two factors—sufficiently low interfacial tension and its rapid increase with decrease in particle radius[19].

Micelle formation can be regarded thermodynamically as resembling the formation of a new phase, with the c.m.c. as saturation concentration[12]. However, the resulting micelles do not coalesce into a continuous phase, but are uniformly distributed in the aqueous medium, forming a "pseudophase". Micelle formation actually possesses several properties characteristic of phase separation. Many properties of surfactant solutions undergo an abrupt change at the critical micelle concentration (see above). The increase in solubility of certain substances in surfactant solutions above the c.m.c. can be regarded as similar to dissolution of the substance in a separate phase. At the Kraft point—the temperature above which micelle formation is possible—the first derivative of the solubility of the surfactant with respect to temperature exhibits a discontinuity, which is also characteristic of one type of phase transition. The variation in the c.m.c. caused by various substances can be regarded, on the basis of the pseudophase model of micelle formation, as variation in the true solubility of the surfactant.

† Several aspects of this problem have already been touched upon in monographs[8,7] or have formed the subject of separate reviews[1,5], many conclusions from which we shall use in the subsequent discussion. The relation between micellar catalysis and processes involving macromolecular catalysts (both synthetic polymers and biopolymers—enzymes) was subjected to detailed examination by Morawetz[5].

Another approach is to describe micelle formation as an equilibrium process using the law of mass action. On this model a sharp change in the properties of the system can be expected only if a sufficiently large number of molecules are bound into the micelle[12,20].

Micelles are dynamic structures having times of formation and destruction of a few milliseconds[21]. Ionic micelles usually comprise roughly 50–100 surfactant ions. In dilute solutions they are supposed to be spheroidal with the polar groups on the surface and the hydrophobic chains at the centre. A spherical micelle is shown diagrammatically in Fig. 1. The ionic "head" groups in the diphilic surfactant molecules and some of the gegenions form a compact Stern layer[22], in which about 60–70% of the micellar charge in neutralised. The remaining gegenions form a diffuse Gouy–Chapman layer. The mean surface potential (the ζ-potential) of the micelle can be estimated from the electrophoretic mobility, although the exact value of ζ depends to some extent on the model used for interpreting the experimental data. It usually varies in the range 50–100 mV. A critical examination of the estimation of surface potential from the shift in pK_a of dyes adsorbed on the micelle showed[23] that the potential measured is rather higher than the ζ-potential but less than the total potential difference between micelle and water.

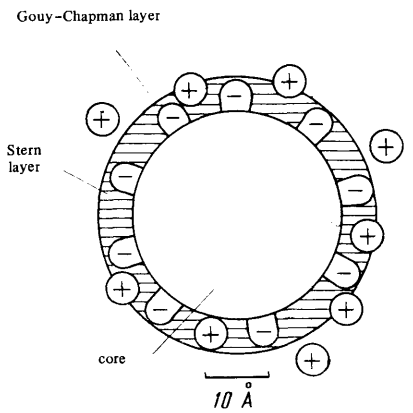


Figure 1. Schematic representation of a micelle of an ionogenic surfactant according to Stigter[22] (micelle of sodium dodecyl sulphate shown as example).

The behaviour of ionic surfactants is greatly complicated by interaction between micelles and gegenions. The concentration of the latter in the aqueous phase can be supposed to remain almost constant and equal to the concentration of molecularly disperse surfactant (i.e. to the c.m.c.[24]) in the vicinity of the critical micelle concentration, but further increase in surfactant concentration is accompanied by an increase in the concentration of gegenions in the water. This tends to depress the c.m.c. and the surface potential of the micelle, and also increase the size and change the shape of the micelles[12,15].

The micellar surface is not uniform[25]. Nuclear magnetic resonance data[26] indicate that some of the hydrocarbon chains are turned towards the solvent, or at least come into contact with it periodically. It must also be borne in mind that micelles contain a considerable quantity of water, e.g. 33–46 vol.% in those of sodium dodecyl sulphate[27]. The water is probably located not only in the surface layer but also in the hydrophobic core of the micelle, the content decreasing with distance from the polar head group into the interior of the micelle[28,29]. On the whole it may be supposed that the micellar surface is a polar environment differing in properties from water itself. For example, the effective dielectric constant of the micellar surface was estimated as 36[30] from the position of the charge-transfer band in the surface layers of micelles formed by dodecylpyridinium iodide.

The hydrophobic core of a micelle is closely similar to a liquid hydrocarbon in properties, although rather more ordered. Results obtained by means of a fluorescent probe group[31] indicate that the core closely resembles a liquid hydrocarbon in nature, although the microviscosity is considerably higher in micelles than in hydrocarbons. The whole micelle, although evidently possessing some solid character[32], is more in the liquid state. This last view is consistent with the facts (*a*) that micelle-forming ions are able to form mixed micelles with various additives[12], and (*b*) that solubilisation takes place in micellar systems. This process resembles in many respects the extraction of organic substances from an aqueous phase, with the micelles acting as the second phase.

2. Distribution of Simple Substances between Aqueous and Micellar Phases

A specific feature of solutions of surface-active agents is their ability to dissolve within the micelles substances that are sparingly soluble in water, with the formation of thermodynamically stable isotropic solutions[12,33,34]. This explains the sharp increase in solubility of certain substances when the critical micelle concentration is reached in a surfactant solution (the phenomenon of solubilisation). With further increase in the surfactant concentration the solubility increases in proportion to the latter, mainly because of the increase in the total number of micelles in unit volume. Solubilisation is affected by the many factors which in turn influence the properties of micelles (temperature, presence of foreign non-electrolytes, concentration of gegenions), and is further complicated by the effect of the solubilised substance itself on the micelles[35]. Nevertheless, data on solubilisation can be analysed with some caution by means of a simple model, in which micelles are regarded as a separate phase from the rest of the solution[36].

We postulate that a solute A is distributed between micellar and aqueous phases in conformity with the simple distribution law:

$$[A]_M/[A]_W = P_A \qquad (1)$$

Here and subsequently the subscripts "M" and "W" denote quantities relating to micellar and aqueous phases respectively. The total concentration of A, averaged over the volume of the whole system, is

$$[A]_0 = [A]_M CV + [A]_W(1 - CV), \qquad (2)$$

which with (1) gives

$$[A]_0/[A]_W = 1 + (P_A - 1)CV, \qquad (3)$$

where C is the surfactant concentration (molarity) less the c.m.c., and V is the molar volume of the surfactant, the factors CV and $1 - CV$ being the fractions by volume of micellar and aqueous phases respectively. Provided that the distribution (1) is satisfied at concentrations up to S_W, the solubility of A in pure water, its solubility $S_{M,W}$ in the

presence of the surfactant is related to S_W by Eqn. (3), which can be conveniently written

$$S_{M,W}/S_W = 1 + K_A C, \quad (4)$$

where the constant K_A is given by

$$K_A = (P_A - 1)V \quad (5)$$

and thus has the dimensions (M^{-1}) of an ordinary binding constant. From general considerations, however, Eqn. (1) would be satisfied only for dilute solutions. Therefore Eqn. (4) is applicable only to sufficiently sparingly soluble substances, whose saturated solutions can still be regarded as dilute.

(*a*) Determination of binding constants of solutes with micelles

Binding constants of type K_A are convenient measures of efficiency of solubilisation. Examples of the use of solubilisation data for various substances to determine their binding constants with micelles can be found in Refs. 36–40. Fig. 2[4] shows plots of Eqn. (4) illustrating the typical dependence of the solubility of several *p*-nitrophenyl carboxylates on surfactant concentration. A more general method applicable to substances whatever their solubility is to determine their binding with the micelles by gel filtration[40]. However, this method is restricted to fairly large partition coefficients ($P \geqslant 10$).

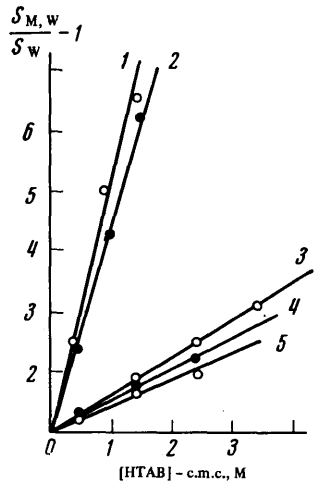


Figure 2. Effect of hexadecyltrimethylammonium bromide on solubility of *p*-nitrophenyl carboxylates: 1) heptanoate; 2) β-phenylpropionate; 3) salicylate; 4) butyrate; 5) αα-dimethylpropionate[4].

The binding constant of a substance with a micelle can readily be found also when the variation in some molecular property on passing from water to the micellar medium can be followed. Such properties may be the visible and ultraviolet spectra[41], the nuclear magnetic resonance[42] and electron spin resonance[43] spectra, or also e.g. the reactivity towards solvolysis[37,38,44]. Since their variation is connected with the change in the microenvironment in the vicinity of the molecule undergoing solubilisation, data of this type can be used to solve the important problem of the arrangement of the solubilised molecule in the micelle.

(*b*) Location and orientation of solubilised molecules in micelle

A solute can be arranged in various ways in the micelle: it may pass completely inside the hydrophobic core, or penetrate a particular depth into the surface layer; it can be adsorbed on the surface of the micelle or—what is most probable for molecules containing polar substituents—be oriented with the polar portion of the molecule situated in the surface layer and the non-polar portion directed into the micelle. In order to solve the problem of where a solubilised molecule had entered—into the hydrophobic core or into the hydrated surface layer—it was usual to compare the spectra (ultraviolet, e.s.r., n.m.r.) observed in the presence of the detergent with the spectra in water and in an organic solvent (hydrocarbon, alcohol). However, the interpretation of such results is usually complicated, because the observed effects may depend on various factors.

An instructive example is the investigation of the polarity of the sorption centre in the enzyme α-chymotrypsin, on which the colorant proflavin is bound. The "red shift" of the visible absorption spectrum of proflavin on interaction with the enzyme was interpreted as resulting from the low polarity of the sorption site in the protein globule, since the same shift occurs in aqueous dioxan[45]. It has since been shown[46], however, that the shift in λ_{max} of proflavin is determined not by the dielectric constant of the medium but by the refractive index. Thus the shift relative to water ($\epsilon = 81$ and $n_D = 1.33$) is the same in dioxan (2.4 and 1.42) and in formamide (109.5 and 1.44). Detailed analysis of the spectral changes undergone by proflavin in various systems suggests[46] the presence of orientation interaction in its complex with chymotrypsin on excitation of the colorant molecule, and hence that the corresponding sorption site in the enzyme is highly polar.

Parallel studies by several methods of the arrangement of solubilised molecules in the micelle[47,48], giving consistent results, are therefore especially valuable. In general aliphatic molecules or side-chains are immersed in the hydrophobic core of the micelle[12,49]; aromatic molecules or parts thereof are probably (but not always[50]) situated in the surface layer of cationic micelles[49], but in the hydrophobic core of anionic and non-ionic[50,51] micelles. Molecules with polar substituents (alcohols, phenols, acids, amines, etc.) are oriented with their polar groups in the surface layer and the non-polar portions immersed in the core[12,47]; ions are adsorbed on the surface of the micelles[12,22].

The efficiency of chemical interaction between solubilised molecules should obviously be strongly dependent on their mutual orientation. The arrangement of solubilised molecules in the micelle must therefore be examined in rather greater detail.

The most widely used method for investigating the microenvironment of solubilised molecules is n.m.r. spectroscopy‡, for the chemical shifts of protons and

‡ The lifetime of solubilised molecules in micelles has also been estimated from n.m.r. spectral data. That of the benzene molecule in micelles of sodium dodecyl sulphate was determined[42] as ~ 10^{-4} s from the broadening of the n.m.r. band of benzene on solubilisation.

especially fluorine-19 atoms are fairly sensitive to the medium. Muller and Birkhahn[52] suggested as a quantitative measure of the closeness of the environment of a molecule to a liquid hydrocarbon the function

$$Z=(\delta_M-\delta_W)/(\delta_{HC}-\delta_W) \quad (6)$$

where δ_M, δ_W, and δ_{HC} are the chemical shifts of hydrogen or fluorine atoms in the test molecule solubilised by micelles and in aqueous and hydrocarbon solutions. The quantity Z can obviously be calculated also from ultraviolet, visible, or e.s.r. spectroscopic data. The Table gives values for benzene and certain derivatives in the presence of a number of surfactants. Sufficiently reliable interpretation of Z is evidently possible only in comparative experiments examining the variation in Z resulting from variation in some parameter of the system, whereas the absolute value of Z may firstly contain a systematic error[28] and secondly be a non-linear function of the composition of the medium.

Values of Z for aromatic molecules solubilised by micelles of various surfactants[51].

Surface-active agent	Z	Substance
Polyoxyethylene dodecyl ether	0.06-0.16	benzene
Hexadecyltrimethylammonium bromide	0.18	benzene
Sodium dodecyl sulphate	0.20-0.22	radicals I and II
Sodium laurate	0.52	trifluoromethylbenzene
Sodium decanoate	0.29-0.33	benzene
Sodium decanoate + 1 M NaCl	0.55	benzene

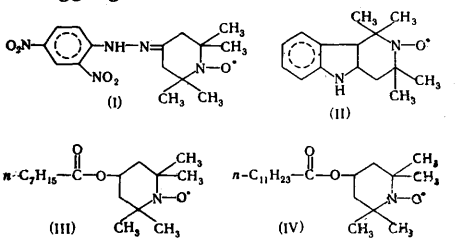
Important information on the nature of solubilisation can be obtained simply by comparing the position of the chemical shift of the solubilised molecule with the position in aqueous and hydrocarbon solutions. Such investigations[49] suggest that aromatic molecules are arranged in the surface layer of the cationic micelles n-hexadecyltrimethylammonium bromide, whereas aliphatic molecules and aliphatic side-chains of aromatic molecules enter the hydrocarbon core. The shielding constants of the fluorine nuclei in *para*-substituted fluorobenzenes (with formyl, acetyl, methoxyl, trimethoxymethyl, and diethoxymethyl as substituents) show that these molecules are arranged in the micelles of sodium dodecyl sulphate in such a way that the hydrogen bonds with water are preserved[53]. From this it might be concluded that these molecules are located in the surface layer of the micelle, but since water may be partly enclosed also in the inner regions of the micelle (see above), they may nevertheless be immersed to some extent in the hydrophobic core.

The permeability of micelles for molecules of substances possessing no well defined hydrophobic properties can be studied by means of the n.m.r. spectra of fluorine present in the surfactant (sodium 12,12,12-trifluorododecyl sulphate)[54]. Glycerol, glycine, and urea hardly penetrate the hydrocarbon core of the micelle at all; methanol and acetamide enter only to a slight extent; and ethanol, acetone, and dioxan freely enter the inner regions of the micelles.

The ultraviolet and visible spectra of solubilised molecules can be used only with aromatic compounds. Reigelman et al., in their pioneering work[50], were the first to pose the problem of determining the site of a solubilised molecule in a micelle. In their view four modes of solubilisation—penetration into the hydrocarbon core, deep immersion in the surface layer, shallow immersion in the surface layer, and adsorption on the micelle surface—must be distinguished. They investigated the nature of solubilisation in micelles of three types of surfactants—anion-active (potassium laurate), cation-active (dodecylammonium chloride), and non-ionic (Brij 35—oxyethylated dodecanol). From an analysis of the fine structure and the positions of the maxima in the spectra of several aromatic compounds they concluded that solubilised molecules are arranged in the same way in all three types of micelles: ethylbenzene penetrates into the hydrocarbon core; naphthalene, anthracene, and *trans*-azobenzene are deeply immersed in the surface layer; *o*-nitroaniline effects shallow penetration of the surface layer; and dimethyl phthalate is adsorbed on the surface of the micelles.

A more quantitative result was obtained by Rehfeld[41], who studied the solubilisation of benzene in the presence of sodium dodecyl sulphate. The spectrum of the solubilised benzene, whose concentration in the micelle was 0.47 ppm, was roughly equivalent to the spectrum of a solution of benzene in hydrocarbons and dodecanol or methanol at a concentration of 0.5 ppm. Certain differences in the spectra were due, according to this author, to various non-equivalent positions of the benzene molecule in the micelle, between which dynamic equilibrium was rapidly established.

Investigations using electron spin resonance require that the molecule undergoing solubilisation shall contain a "paramagnetic label", for which purpose iminoxyl radicals have been widely used[55]. The e.s.r. spectra of the "label" enable at least the following information to be obtained—concentration of radicals, polarity of solvent surrounding the radical, rotational mobility of radical, and degree of aggregation of radicals§.



Solubilisation of the radicals (I)–(IV) by micelles of sodium dodecyl sulphate has been investigated by Waggoner and his coworkers[57]. Since both ends of radicals (I) and (II) can be watched (one end by means of the e.s.r. spectra and the other by the ultraviolet spectra), these workers attempted to distinguish three situations—adsorption on the micelle surface, radial orientation in the micelle, and submersion in the hydrocarbon core—but the results were consistent with none of these static models of solubilisation. It was therefore concluded that the observed parameters were mean values resulting from rapid exchange between the different positions, and on the average the radicals were in a fairly polar environment. Data on radicals (III) and (IV) also indicate that the solubilised molecules are subject to relatively rapid rotational motion.

Information on the nature of the bonding of solubilised molecules by micelles was obtained also by studying the effect of salts on solubilisation. Additions of salts lower the degree of solubilisation of octanol and benzaldehyde by

§ A critical survey has been published[56] of factors complicating the interpretation of e.s.r. spectra of solubilised radicals.

hexadecylpyridinium[58], and of dimethyl phthalate by potassium laurate and Triton X[59] (oxyethylated octylphenol). This indicates that solubilised molecules of these substances interact with polar groups of the surfactant molecules. On the other hand, the solubilisability of octane and benzene by hexadecylpyridinium increases in the presence of salts[58], which is interpreted as a change in structure of the micelles produced by the salts, although this phenomenon can probably be explained as an ordinary salting-out effect.

The above brief review shows that the interrelation between the molecular structure of organic compounds and their arrangement and orientation in the micelle on solubilisation cannot yet be regarded as adequately studied. A future kinetic study of organic reactions occurring in micelles may reveal fine effects of micellar structure and the orientation of solubilised molecules.

(*c*) Nature of interactions during solubilisation and free energy of transfer from water into the micelle

Hydrophobic and ionic interactions with non-polar and charged groups of the solubilised molecules are responsible for binding to micelles[12,33,34,60]. In the case of aromatic molecules interaction between charged groups in the micelle surface and the π-electron system of the aromatic ring also plays a part[49]. We give some very rough estimates of the partition coefficient P to be expected for various types of molecules. We start from the usual relation for the equilibrium constant

$$P = e^{-\frac{\Delta\mu_0}{RT}} \qquad (7)$$

where $\Delta\mu_0$ is the change in the standard chemical potential of the partitioned substance on passing from water to the micelle.

If a molecule is bound to a micelle mainly by hydrophobic interactions, $\Delta\mu_0$ can be either calculated theoretically[61,62] or estimated from data on the free energy of transfer of the molecule from water to a non-aqueous solvent, e.g. octanol[60,63]. The correctness of such estimate is confirmed in particular by data[36] showing that the partition coefficients of several dyes between the micelles of a non-ionic surfactant (Triton X-100) and water are close to the values for these dyes between octanol and water. We have found that the increment in the free energy of transfer of an aliphatic or a phenylalkyl group from water into the micelle of a cation-active surfactant (hexadecyltrimethylammonium bromide) is practically equal to the increment for transfer of the same group from water to n-octanol[4] (0.6–0.7 and 2.9 kcal mole^{-1} for a methylene group and for benzene respectively). The latter value yields for benzene $P \simeq 100$; experimental data give calculated values of $P = 75$ and 280 for sodium dodecyl sulphate[41] and for hexadecyltrimethylammonium bromide[64].

The contribution of the electrostatic interaction of an ion or an ionic group in a molecule with the micellar charge of an ionogenic surfactant can be estimated from the expression for the electrostatic free energy $Ze\Psi$, where Z is the ionic charge, e the electronic charge, and Ψ the surface potential of the micelle[12]. If Ψ is expressed in millivolts, as is usual, the contribution of electrostatic interaction to the partition coefficient can be written $\exp(-Z\Psi/25.2)$ (at 20°C).[65] With the usual values of the ζ-potential of 50–100 mV (see above) this factor is 10–50. However, the actual potential at the site of a solubilised molecule is usually higher than the ζ-potential[23].

The energy of interaction with dipolar molecules, even those possessing large dipole moments (e.g. Zwitterionic amino-acids), is probably insignificant, and for systems of this type (interaction of amino-acids with macroions) is comparable with RT.[66]

III. KINETICS OF CHEMICAL REACTIONS IN THE PRESENCE OF MICELLES OF SURFACE-ACTIVE AGENTS

In the discussion of the kinetics of micellar reactions the micelle M is most often regarded[2] as an additional species, which on combination with a reactant A can change its reactivity both in a unimolecular reaction and on reaction with another substance B dissolved in water:

$$\begin{array}{ccc} A + M & \overset{K}{\rightleftharpoons} & AM \\ \downarrow k_W[B] & & \downarrow k_M[B] \\ \text{Products} & & \text{Products} \end{array} . \qquad (8)$$

The association constant in (8) has its usual significance ($K = [AM]/[M][A]$), while k_W and k_M are the conversion rate constants of A in water and in the micelle. The effective reaction rate constant measured experimentally (as the ratio of the rate of the process to the total concentration of the reactant: $k_{exp} = v/[A]_0$) depends in this case on the surfactant concentration:

$$k_{exp} = \frac{k_W + k_M[M]}{1 + K[M]} . \qquad (9)$$

provided that $[M] \gg [AM]$. The concentration of the micelles is given by the ratio $[M] = C/N$, where N is the aggregation number.

According to the principles discussed in Section II, however, the binding of the reactant molecules to the micelles involves physically a partition of the substance between micellar and aqueous phases rather than association in the stoichiometric proportions 1 : 1. In other words, the kinetic scheme of the reaction must be written differently:

$$\begin{array}{ccc} (A)_W & \overset{P}{\rightleftharpoons} & (A)_M \\ \downarrow k_W[B] & & \downarrow k_M[B] \\ \text{Products} & & \text{Products} \end{array} \qquad (10)$$

where the partition coefficient P is given by Eqn. (1). When the surfactant concentration greatly exceeds the reactant concentration, the two approaches lead to formally indistinguishable kinetic equations. A formula for the effective rate constant based on scheme (10) was probably first given by Grunwald[67]:

$$k_{exp} = \frac{k_W + k_M P \varphi_M}{1 + P\varphi_M} \qquad (11)$$

where the volume fraction of the micellar phase $\varphi_M \ll 1$. Since $\varphi_M = [M]NV$, a relation can easily be established between the equilibrium constants in Eqns. (9) and (11):

$$K = P \cdot N \cdot V \qquad (12)$$

Equations (9) and (11) are quite correct for first-order reactions, but there are fundamental objections to their application to higher-order reactions. With a bimolecular reaction, in fact, the constant k_M in these equations has the significance of a rate constant for interaction of one reactant, attached to the micelle, with the other, unattached reactant, uniformly distributed throughout both phases. However, the latter condition can hardly be satisfied in general, since the second reactant may also

interact with the micelle, and will then have different concentrations in aqueous and micellar phases. In this case, moreover, the fractions of the second reactant in aqueous and micellar phases would depend on the concentration of micelles, so that in principle Eqns. (9) and (11) give an incorrect dependence of k_{exp} on the surfactant concentration. This is evident from the monotonic increase in k_{exp} with the volume fraction of the micellar phase indicated by Eqn. (9): actually, the dependence of k_{exp} on C observed experimentally for a bimolecular reaction usually passes through a maximum[1]. The occurrence of an optimum surfactant concentration is easily explained (see below) if the distribution of the second reactant is taken into account.

The situation is simpler in the particular case in which the second reactant has a very high concentration (in comparison with the surfactant) or is a component of a buffer solution. Its concentrations in micellar and aqueous phases then remain almost constant but are unequal and are independent of the surfactant concentration. As a consequence, Eqns. (9) and (11) give a correct formal description of the dependence of k_{exp} on the surfactant concentration. In comparing the constants k_M found by means of these equations with the constants k_W, however, we must bear in mind that the former are effective values, since they contain the ratio of the concentrations of the second component in water and in the micelle.

The effect of micelles on the kinetics of bimolecular reactions when both reactants are bound to the micelle has been discussed qualitatively by Heitmann[68]. A quantitative treatment of this concept and its experimental verification have been undertaken by the Reviewers[4,69], and will be considered in detail below.

1. Kinetic Concept of Micellar Effects in a Bimolecular Reaction

Regarding a surfactant solution above the critical micelle concentration as a two-phase system, in conformity with the above discussion, we can express the observed reaction velocity v, averaged over the whole volume of the system, in terms of the reaction velocities in micellar and aqueous phases v_M and v_W:

$$v = v_M CV + v_W(1 - CV) = k_{exp}\,[A]_0[B]_0. \qquad (13)$$

Assuming that the law of mass action is satisfied in each phase, we obtain

$$\left.\begin{aligned} v_M &= k_M [A]_M [B]_M \\ v_W &= k_W [A]_W [B]_W \end{aligned}\right\}. \qquad (14)$$

The relation between the total concentrations of the reactants $[A]_0$ and $[B]_0$ and their true concentrations in the corresponding phases is established by means of Eqns. (1) and (2) for each reactant. This involves the postulate that the equilibrium distribution of the reactants between the phases is not displaced by the occurrence of the chemical reaction. The justification is that the exchange of molecules between the phases occurs very rapidly (see above). From Eqns. (1), (2), (13), and (14) it follows that

$$k_{exp} = \frac{k_M P_A P_B CV + k_W(1 - CV)}{(1 + K_A C)(1 + K_B C)} \qquad (15)$$

where the constants K_A and K_B are defined by formula (5).

Molecules of the same kind can in general be differently arranged and oriented in the micelle (above). The observed effective rate coefficient k_M is therefore in fact "averaged" over the volume of the micelle. We consider as a limiting case the situation in which the observed reaction velocity includes not only the rates in micellar and aqueous phases but also the rate of a reaction between solubilised and unsolubilised reactants:

$$v = k_M [A]_M [B]_M CV + k'_M [A]_M [B]_W CV + k''_M [A]_W [B]_M CV + k_W [A]_W [B]_0 (1 - CV)$$

whence we obtain

$$k_{exp} = \frac{(k_M P_A P_B + k'_M P_A + k''_M P_B) CV + k_W(1 - CV)}{(1 + K_A C)(1 + K_B C)}$$

This equation is similar in form to (15), and when P_A, $P_B \gg 1$ (strong binding of reactants) and $k_M \simeq k_M' \simeq k_M''$ it shows approximately the same dependence of k_{exp} on P_A, P_B, and C as does Eqn. (15).

In the case of dilute surfactant solutions, in which the volume fraction of the micellar phase is small, Eqn. (15) can be simplified to

$$k_{exp} = \frac{k_M P_A P_B CV + k_W}{(1 + K_A C)(1 + K_B C)}. \qquad (16)$$

This equation¶, first given in Ref. 69, enables the nature of micellar effects to be analysed as functions of the relation between the "elementary" rate constants in the two phases and the binding constants of the reactants. We shall consider some important particular cases.

Case 1. Both reactants are weakly bound to or are repelled from the micelle: i.e. P_A, $P_B \leq 1$. Then K_A and K_B vary from zero to $-V$, and when $C < 0.1$ M (corresponding to dilute surfactant solutions) we have

$$k_{exp} \cong k_M P_A P_B CV + k_W. \qquad (17)$$

In this case an appreciable increase in k_{exp} in comparison with k_W is possible only with $k_M \gg k_W$, since $CV \ll 1$. In rare cases, however, k_M exceeds k_W hundredfold, but usually $k_M \simeq k_W$ (see below). Even in the most favourable case (when $P_A \simeq P_B \simeq 1$ and at higher surfactant concentrations of ~ 0.1 M), therefore, k_{exp} is able to exceed k_W only about fourfold, since for the usual surfactants V is around 0.3 M^{-1}.[4,6,70] Evidently this case is in general of no special interest.

Case 2. One reactant is strongly bound to the micelle, while the other is weakly repelled from it. This implies e.g. that $P_A \gg 1$, while $P_B \leq 1$. In this case Eqn. (16) can be simplified to

$$k_{exp} = \frac{k_M P_A P_B CV + k_W}{1 + P_A CV} \qquad (18)$$

since from (5) we have $K_A \simeq P_A V$. If the reactant B is very strongly repelled from the micelle $P_B \simeq 0$, or the reaction rate constant in the micelle is small $k_M \simeq 0$, the micelles inhibit the reaction, since in this case k_{exp} would fall with increase in C:

$$k_{exp} \approx \frac{k_W}{1 + P_A CV}. \qquad (19)$$

If, however, $P_B \simeq 1$, it follows from (18) that $k_{exp} \simeq k_W$ in the absence of a specific effect of the micelles on the reaction, i.e. with $k_M \simeq k_W$, and therefore the reaction

¶ When the reactant concentrations are far smaller than the surfactant concentration, the concept of a distribution of the reactants between micellar and aqueous phases and the less rigorous hypothesis of association of reactants with micelles give the same results. We have already seen this for a first-order reaction. The mathematics for a second-order reaction is similar.

velocity is almost independent of the presence of the surfactant. But when $k_M > k_W$, or conversely $k_M < k_W$, increase in C produces an increase or conversely a decrease in k_{exp}, in conformity with the equation

$$k_{exp} \approx \frac{k_M P_A CV + k_W}{1 + P_A CV} \qquad (20)$$

and in both cases k_{exp} reaches the limiting value k_M.

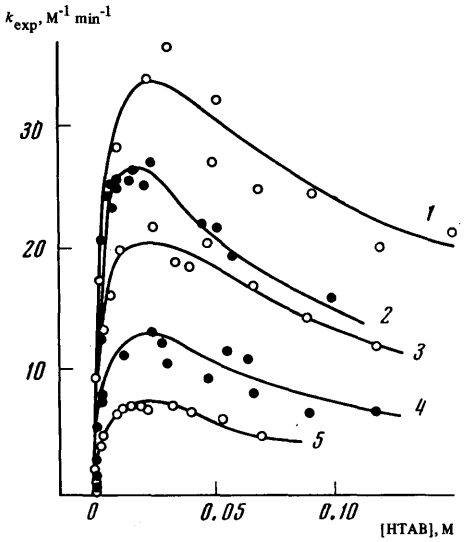


Figure 3. Dependence of experimental rate constant for reaction between fluoro-2,4-dinitrobenzene and the methyl ester of *N*-benzoyl-L-histidine on surfactant concentration at various temperatures (°C): 1) 55; 2) 48; 3) 40; 4) 32; 5) 25.[71]

Case 3. The case in which both reactants are strongly bound to micelles is of especial interest. Considerable acceleration of the reaction is now possible in the presence of surfactant micelles even if they have no specific influence on reaction velocity. The reason is that the reactants become concentrated in the micellar phase. When P_A, $P_B \gg 1$, Eqn. (16) can be written

$$k_{exp} = \frac{\bar{k}_M K_A K_B C + k_W}{(1 + K_A C)(1 + K_B C)} \qquad (21)$$

where

$$\bar{k}_M = k_M / V. \qquad (22)$$

If the reaction hardly occurs at all in the micelle ($k_M \simeq 0$), the micelles have an inhibiting effect, since k_{exp} falls monotonically with increase in C:

$$k_{exp} \cong \frac{k_W}{(1 + K_A C)(1 + K_B C)}. \qquad (23)$$

In all the remaining cases in which reaction is accelerated in the presence of micelles, the dependence of k_{exp} on C passes through a maximum (Fig. 3 illustrates a typical case). The physical significance of the presence of an optimum is that increase in the volume of the micellar phase is accompanied both by an increase in the quantity of substance passing into it from water and by a decrease in the concentration of this substance in the micellar phase. The first process tends to accelerate the reaction by increasing the relative proportion of the more rapid micellar reaction, and it predominates at low surfactant concentrations, while the quantity of substance passing into the micelles is small. The second process—dilution of the reactants in the micellar phase—slows down the reaction, and predominates at high surfactant concentrations, when the reactants are mainly present in the micellar phase.

This aspect can be analysed in greater detail for the most important particular case, in which the reaction velocity in the aqueous phase can be neglected. Putting $\bar{k}_M K_A K_B C \gg k_W$, we can then simplify Eqn. (21), and obtain the formula[4]

$$C_{opt} = (K_A K_B)^{-1/2} \qquad (24)$$

for the optimum surfactant concentration, corresponding to the maximum value of k_{exp}. The maximum acceleration of the reaction is then

$$(k_{exp}/k_W)_{max} = \frac{k_M}{k_W} \frac{K_A K_B}{V(\sqrt{K_A} + \sqrt{K_B})^2}. \qquad (25)$$

The ratio k_M/k_W represents the change in reactivity when the reactants are transferred from water into the micelle, and hence the specific effect of the micelles on the transition state of the reaction. The factor following the ratio on the right-hand side of (25) represents the "trivial" acceleration produced by the localisation of the reactants in the micelle.

2. Shift in pK_a of Ionogenic Reactant in presence of Surfactant Micelles

Acceleration or retardation of a reaction may also be caused by a shift in the pK_a of an ionogenic reactant in the presence of micelles. General consideration has already been given[4] to the kinetics of a bimolecular reaction involving an ionogenic reactant. Taking into account the dissociation of the reactant

$$AH \overset{K_a}{\rightleftharpoons} A^- + H^+ \qquad (26)$$

and assuming that the reactive form is, for instance, the anion

$$A^- + B \xrightarrow{k_W^0} \text{Products} \qquad (27)$$

we can write the effective rate constant of the reaction in the form

$$k_W = k_W^0/(1 + [H^+]_W/K_a). \qquad (28)$$

Formally the same relation applies in the presence of a surfactant:

$$k_{exp} = k_{exp}^0/(1 + [H^+]_W/K_{a,exp}), \qquad (29)$$

where

$$k_{exp}^0 = \frac{\bar{k}_M^0 K'_A K_B C + k_W^0}{(1 + K'_A C)(1 + K_B C)} \qquad (30)$$

and

$$K_{a,exp} = K_a \frac{1 + K'_A C}{1 + K_A C}. \qquad (31)$$

Here K_A and K'_A are the binding constants of undissociated and ionic forms of the reactant A, and K_B is the binding constant of reactant B. Analysis of Eqn. (29) yields for

the maximum acceleration of the reaction the expression[4]

$$(k_{exp}/k_W)_{max} = \frac{k_M}{k_W}\frac{K_A K_B}{V(\sqrt{K_A}+\sqrt{K_B})^2}\frac{K'_A}{K_A} \quad (32)$$

As with the simpler equation (25), the second factor on the right-hand side represents the localisation of the reactants (substance B and the non-ionic form of A) into the micellar phase. The last factor on the right-hand side of Eqn. (32) represents the effect of the shift in the pK_a of the ionogenic reactant in the presence of the micelles, as can be seen from Eqn. (31), whence it follows that $K_{a,exp}/K_a$ tends to K'_A/K_A at sufficiently high values of C. With a cationic micelle, which would obviously bind the anion A^- more strongly than the non-ionic form A, we have $K'_A > K_A$, so that the shift in pK_a makes an additional contribution to the acceleration of the reaction in the presence of micelles (this effect is discussed in greater detail in Ref. 4).

3. Determination of Binding Constants of Reactants with Micelles from Kinetic Data. Experimental Determination of Second-order Rate Constant in Micellar Phase

It is a simple matter to analyse the dependence of the rate of a first-order reaction on C, for which purpose we convert Eqn. (11) to the form

$$k_{exp} = \frac{k_M P_A C V + k_W}{1 + P_A C V} \quad (33)$$

on the assumption that $\varphi_M = CV$. The value of k_M can then be found as the limiting dependence of k_{exp} on C at high C, and the binding characteristic of the reactant PV as the reciprocal of the abscissa for which $k_{exp} - k_W$ has half its limiting value. Graphical methods, based on the linearisation of Eqn. (33), are normally used[2] to evaluate k_M and PV.

Binding constants of reactants with micelles and the true reaction rate constant in the micellar phase can also be found for a bimolecular reaction. We shall consider this for one of the most important particular cases of micellar catalysis†, when $k_M K_A K_B C \gg k_W$. For this purpose we write (21) in the form

$$C/k_{exp} = \alpha + \beta C + \gamma C^2, \quad (34)$$

where

$$\alpha = 1/k_M K_A K_B,$$
$$\beta = \alpha(K_A + K_B),$$
$$\gamma = \alpha K_A K_B. \quad (35)$$

A graphical method is convenient for determining α, β, and γ from experimental data. The value of α is then the intercept made on the vertical axis by the curve representing the dependence of C/k_{exp} on C according to Eqn. (34). With α determined, the experimental results are conveniently plotted as the linear equation

$$\frac{C/k_{exp} - \alpha}{C} = \beta + \gamma C \quad (36)$$

which follows from (34). The intercept on the vertical axis and the slope of the straight line obviously give β and γ respectively. Finally, knowing α, β, and γ, we can use Eqns. (35) to calculate the required quantities K_A, K_B, and k_M.

A study[71] of the effect of cationic micelles of hexadecyltrimethylammonium bromide on the aminolysis of fluoro-2,4-dinitrobenzene by *N*-benzoyl-L-histidine has shown[71] agreement between the binding constants of the reactants with the micelles K_A and K_B found by the above method from kinetic data and measurements in an independent experiment on the solubilisation of the reactants by the micelles. Such agreement proves the correctness of the above kinetic concept of micellar effects in bimolecular reactions.

The molar volume V of the surfactant must be known in order to calculate the true rate constant k_M of a bimolecular (but not a unimolecular) reaction in the micellar phase from the measured effective value $\bar{k}_M$. This independent parameter must be known also in order to calculate partition coefficients P from experimental binding constants K. Certain difficulties arise as a consequence, since the molar volume V occurring in Eqn. (5) or (22) is in fact an effective quantity, representing that portion of the surfactant molecule which forms the region of the micelle where the reactants are actually solubilised and the chemical reaction takes place. However, difficulties already arise in estimating the total molar volume of the surfactant. The estimation usually starts[4,6,40] from the density of the micelles calculated from the partial specific volume of the surfactant above the critical micelle concentration, which varies from 0.9 to 1.1 g ml^{-1} for different surfactants[70]. On this basis an estimate of the total molar volume of the surfactant in the micelles which started from a density of ~ 1.0 g ml^{-1} might have been regarded as quite acceptable. However, this density applies to the "dry" surfactant, and does not allow for the hydration of the micelles, which is very considerable (see above). Nevertheless, the use of such a value for the density of the micelles probably does not lead to serious errors.

As example we estimate the size of micelles of the well studied sodium dodecyl sulphate[22,25]. The probable radius of the hydrocarbon core of its spherical micelles is 16.6 Å, the thickness of the Stern layer 4.6 Å, and the aggregation number 62. Hence the volume of the whole micelle is 4.0×10^4 Å^3,[5] or the molar volume of the surfactant in the micelles is 0.4 M^{-1}. Using the molecular weight 288 and density of the "dry" surfactant in the micelles 1.1 g ml^{-1},[70] we find that the corresponding molar volume is 0.26 M^{-1}. Since sodium dodecyl sulphate micelles contain 33 vol.% of water[27], the molar volume of the hydrated surfactant in the micelles is 0.39 M^{-1}, almost identical with the estimate obtained above from the dimensions of the micelles.

Estimating the effective molar volume is a more complicated task. All the reactions that have hitherto been studied in the presence of micelles involve polar molecules, which on solubilisation are probably located in the surface layers of the micelles. In most cases the reaction is assumed to occur in some surface region of the micelle, which covers the Stern layer and a further 3–4 methylene groups of the hydrocarbon chain in the surfactant molecule[1]. In the case of sodium dodecyl sulphate this means that ~ 4 Å must be added to the 4.6 Å thickness of the Stern layer. The volume of such a layer is 3.6×10^3 Å^3, which gives a molar volume of 0.32 M^{-1}, only slightly less than the above estimate of the total molar volume of the surfactant. It may be expected that this difference will also be small in the remaining cases.

† A general analysis of Eqn. (21) has been given previously[71]. The general equation (16) is analysed similarly to (21).

4. Micellar Catalysis in Reactions of the *n*th Order

The contribution made by concentrating the reactants to accelerating the reaction should increase with increase in the kinetic order of the reaction. We can show this for the *n*th-order reaction

$$nA \rightarrow \text{Products}, \qquad (37)$$

When the concentrating effect in the micellar phase is strongly marked ($P_A \gg 1$), while the surfactant concentration is not too large ($CV \ll 1$), the effective reaction rate constant $k_{exp} = v/[A]_0^n$ is given by[8]

$$k_{exp} = \frac{k_M P_A^n CV + k_B}{(1 + P_A CV)^n}. \qquad (38)$$

With $n = 1$ the dependence of k_{exp} on the surfactant concentration tends to the limiting value k_M. With other values of n this function has a maximum. With sufficiently large accelerations, when the rate of reaction in the aqueous phase can be neglected $k_M P_A^n CV \gg k_W$, the optimum surfactant concentration is‡

$$C_{opt} = 1/P_A V(n-1). \qquad (39)$$

At this surfactant concentration the maximum acceleration reaches[8]

$$(k_{exp}/k_W)_{max} = \frac{k_M}{k_B} \cdot \frac{(n-1)^{n-1}}{n^n} P_A^{n-1}. \qquad (40)$$

Equation (40) shows that two factors—change in reactivity of A on passing from water to the micellar phase and the concentrating of A into the micelle—are responsible for accelerating the reaction. The first factor k_M/k_W depends on the mechanism of the reaction and the orientation of the reactants in the micelle; the second factor is determined [not] only by the partition coefficient of the substance between micelle and water but also by the order of the reaction. Values of P usually lie in the range 10^2–10^3. Then the maximum acceleration due solely to the concentration effect, i.e. with $k_M/k_W = 1$, is shown by Eqn. (40) to lie in the range 10–10^2 for a bimolecular reaction, and 10^3–10^5 for a termolecular reaction.

Since the factor $(n-1)^{n-1}/n^n$ in Eqn. (40) varies only slightly with n, the involvement of each new species in the reaction (i.e. unit increase in the order of the reaction) increases the efficiency of micellar catalysis approximately P-fold. This was confirmed by studying the effect of micelles of sodium dodecyl sulphate on the kinetics of the hydrolysis and the formation of benzylideneaniline[8]

$$C_6H_5NH_2 + C_6H_5CHO \rightleftharpoons C_6H_5N{=}CHC_6H_5 + H_2O. \qquad (41)$$

At pH < 9 this reaction is acid-catalysed, whereas at pH 9–12 its progress is independent of pH. Hence the efficiency of micellar catalysis when the reaction order varies from 1 to 3 could be followed by studying the rates of forward and reverse reactions in various pH ranges. Micelles of sodium dodecyl sulphate were found to produce a 3-fold retardation of the pseudounimolecular (pH-independent) hydrolysis of benzylideneaniline, whereas the pseudobimolecular reaction (acid-catalysed hydrolysis) underwent 20-fold acceleration. The effect of micelles on the bimolecular formation of benzylideneaniline was in turn 3-fold acceleration, but the termolecular (acid-catalysed) reaction was accelerated 125-fold. Thus the efficiency of micellar catalysis increases by factors of 40–60 with unit increase in the order of the reaction. This is consistent with the above kinetic concept, since the partition coefficients of the reactants lie in the same range (P = 30–80).[8]

The facts cited in this Review together with the detailed investigation of the effect of surfactant micelles on the kinetics of several other reactions[1,2] demonstrate that the kinetic concept of micellar catalysis that has been developed has the following merits: (i) the dependence of reaction velocity on surfactant concentration can be correctly described for reactions of different kinetic orders; (ii) the binding constants of reactants with the micelle can be calculated from kinetic data, and the reaction rate constant in the micellar phase can be estimated with satisfactory accuracy; and (iii) the acceleration of the reaction due to the concentrating of reactants in the micelle can be predicted and calculated theoretically.

IV. NATURE OF MICELLAR CATALYSIS

Two types of physicochemical factors—(1) change in reactivity of reactants on transfer from water to the micellar phase and (2) the concentrating of reactants into the micellar phase (Eqn. 25) in the case of reactions of the second and higher orders—can be distinguished as responsible for the efficiency of micellar catalysis. The above effect of the shift in the pK_a of an ionogenic reactant is essentially of the second type, since it represents the preferential concentrating of one ionic form relative to the other. Effects of the first type are characterised by the ratio of the rate constants k_M/k_W and may be caused by the environment (including electrostatic interaction of the transition state of the reaction with the surface charge of the micelle) and by orientation of the reactants in the micelle. The contribution of the concentration effect in accelerating reaction is determined mainly by the strength of ionic and hydrophobic interactions between reactant molecules and micelles (by the partition coefficients of the reactants).

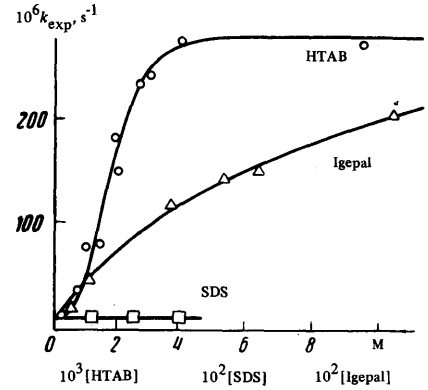
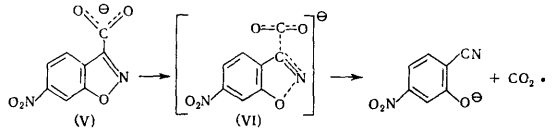


Figure 4. Effect of various surfactants on rate of decarboxylation of the 6-nitrobenzisoxazole-3-carboxylate anion (42).[72]

The most reliable information on the effect of micelles on the true reaction rate constant in the micellar phase

‡ Equations essentially equivalent to (38) and (39) were probably first given in Ref. 9, in connection with the kinetics of emulsion polymerisation.

will be provided by the study of *unimolecular reactions*, when k_M can be found without any assumptions concerning V (see above). Unfortunately, very little work has been done on such reactions. Data obtained by Bunton and Minch[72] on the effects of hexadecyltrimethylammonium bromide (HTAB), the non-ionic surfactant Igepal (an oxyethylated alkylphenol), and sodium dodecyl sulphate (SDS) on the kinetics of the decarboxylation of the anion (V) are plotted in Fig. 4. These workers assume[72] that the catalytic effect of the first of these surfactants is due to the action of the positive charge of the micelle in stabilising the anionic transition state (VI), in which the charge is more delocalised than in the initial species (V):



(42)

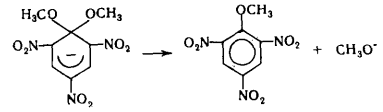
In our view this interpretation is not entirely satisfactory, since firstly it does not explain the catalytic action of a non-ionic surfactant, and secondly it is not entirely clear why a more delocalised charge on the substrate should be subject to stronger electrostatic interaction with the micelle. Probably in this case direct electrostatic interaction with the micellar charge is manifest only in binding the reactant to the micelles. This is indicated by our treatment of the kinetic data (Fig. 4) by means of Eqn. (33). Closely similar values of k_M were obtained for the quaternary bromide and Igepal (2.9×10^{-4} and 3.0×10^{-4} s^{-1}). On the other hand, the binding constants of the initial reactant with the corresponding micelles actually differ substantially (1400 and 20 M^{-1} respectively). The lack of effect of sodium dodecyl sulphate on the reaction is clearly due to electrostatic repulsion of the reactant from the anionic micelle. With cationic and non-ionic micelles the most probable factor tending to increase k_M in comparison with k_W is in our view replacement of the aqueous environment by the comparatively non-polar environment of the micelle. The direction and the magnitude of the observed effect ($k_M/k_W \simeq 100$) are fully consistent with those to be expected for processes involving delocalisation of the charge, and may be due both to stronger hydration of the localised charge in water and to stronger dispersion interaction of the delocalised charge with its environment in the micelle[73,74].

The breakdown of the 2,6-dinitrophenyl phosphate dianion[75]

$$ArOPO_3^{2-} \rightarrow [ArO^- \ldots PO_3^-] \rightarrow ArO^- + PO_3^- \qquad (43)$$

is an analogous process. In the presence of hexadecyltrimethylammonium bromide the reaction is accelerated, with $k_M/k_W = 29$ and $K = 1250$ M^{-1}. The substrate remains almost completely unattached to micelles of a non-ionic surfactant, let alone to an anionic agent; this may explain the lack of effect of non-cationic surfactants on the reaction velocity. The considerable contribution of electrostatic attraction to the efficiency of binding of a doubly charged ion (see above) may be responsible for the absence of binding. However, as in the preceding example, electrostatic interaction between reactant and micellar charge has only a very slight effect on the reaction in the micellar phase. An indication of this is the "competitive" inhibition of micellar catalysis produced by the introduction of gegenions leading to neutralisation of the surface charge on the micelle: i.e. the binding constant decreases, but the rate constant k_M remains almost constant. It is interesting that micelles do not catalyse hydrolysis of the *p*-nitrophenyl phosphate monoanion or the glucose 6-phosphate dianion, which involves transfer of a proton to the resulting negative charge and hence is not accompanied by delocalisation of charge in the transition state.

E. and J. Fendler studied the effect of surfactants on the kinetics of the unimolecular decomposition of Meisenheimer complexes[76]. They examined in greatest detail the reaction



(44)

which is retarded in the presence of hexadecyltrimethylammonium bromide and Igepal, but whose rate is unaffected by sodium dodecyl sulphate. This latter fact is easily explained by electrostatic repulsion of the reactant from the anionic micelle. Although the data given[76] are unfortunately insufficient for detailed analysis of the kinetics, nevertheless even qualitative comparison of the effects observed with different surfactants indicates that here, too, interaction of the substrate with the micellar charge has no decisive effect on the reaction rate constant in the micelle k_M.

The above facts suggest that in general, when the sole difference between initial and transition states is the degree of delocalisation of the charge, the rate constant k_M is mainly affected merely by the change in reaction medium when the reactant passes into the micellar phase. A specific effect of the micellar charge on the rate of a unimolecular reaction can probably be expected only when ionisation occurs in the transition state, as e.g. in the hydrolysis of t-butyl chloride[73].

Most *bimolecular reactions* studied hitherto involve the interaction of appreciably hydrophobic neutral molecules with ions. They comprise mainly the acid and alkaline hydrolysis of carboxylic esters, phosphoric and sulphuric esters, acetals and orthoesters, Schiff bases, and aryl and alkyl halides, as well as nucleophilic substitution of the latter compounds with anions. Data on the effect of micelles on the kinetics of these reactions have been assembled in Ref. 2. The recently investigated reduction of iminoxyl radicals by iron(II) ions[77,78] and the reaction of benzene with the hydrated electron[79] are of the same type. Micellar effects on these processes exhibit several characteristic general features, although there are exceptions[1,2,80]. The reaction is usually accelerated by a surfactant whose micelles are oppositely charged to the reactant ion; when micelles and reactant ions bear like charges, the reaction is inhibited. Non-ionic surfactants generally have no significant influence on the rates of these reactions. The efficiency of ionic surfactants is in turn greatly diminished by increasing the concentration of gegenions.

The simplest explanation of the regularities observed is that a hydrophobic reactant is attached to a micelle by hydrophobic interactions, independently of the charge on the latter. If the second reactant is oppositely charged to the micelle, it also becomes bound to the latter, and thus the reactants are concentrated, which is responsible for accelerating the reaction. If, however, the ion bears a like charge to the micelle, it is repelled from the latter, and reaction is retarded owing to separation of the reactants (Eqn. 19). Since the binding of ions is determined by the surface potential of the micelle, the lowering of the potential with increasing concentration of gegenions tends to diminish the attachment of a reactant ion and hence decreases the efficiency of micellar catalysis.

A fundamental difficulty is encountered when Eqn. (16) is used to analyse the kinetics of these reactions. In fact increase in surfactant concentration is accompanied by an increase in the concentration of gegenions and thus a fall in the surface potential, which entails a decrease in the binding constant for the ionic reactant and a consequent divergence between theoretical and experimental variations of k_{exp} with C (Fig. 5). At large values of C this disregarded effect may be very considerable[8]. The method sometimes used, of maintaining a constant total concentration of gegenions[81], is not entirely correct, since these ions attach to the micelles, so that their concentration in the aqueous phase, which should have been maintained constant, falls with increase in C.

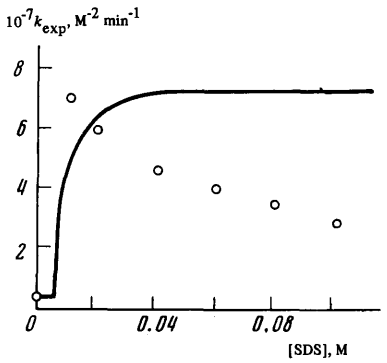
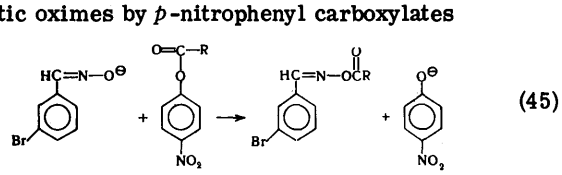


Figure 5. Dependence of experimental rate constant for the acid hydrolysis of benzylideneaniline on concentration of sodium dodecyl sulphate[8]. The theoretical curve has been drawn on the assumption that the surface potential of the micelle remains constant with increase in the surfactant concentration.

The above kinetic concept of micellar catalysis has formed the basis for a most detailed study[4] of the acylation of aromatic oximes by p-nitrophenyl carboxylates



(45)

in the presence of hexadecyltrimethylammonium bromide. Analysis of the experimental results by means of Eqn. (29) shows that the acceleration of the reaction due to the shift in the pK_a of the oxime is about 15-fold. The effect of concentrating the reactants—ester and undissociated form of oxime—in the micellar phase varies from 60 for the acetate to 2000 for the heptanoate. The two effects enable substantial accelerations to be achieved, up to 17 000 in the case of the salicylate.

An extremely interesting dependence of k^0_M/k^0_W on the structure and dimensions of the aliphatic portion of the hydrocarbon radical R has been found in the latter investigation[4] (Fig. 6). Since the mechanism of reaction (45) should not depend on the size of R, so that the same change in reactivity on transfer of the reactants to the micellar phase should be produced by the environment and by interaction with the micellar charge, the most probable reason for the observed dependence of the ratio on the size of the side-chain R may be *orientation of the reactants in the micelle*.

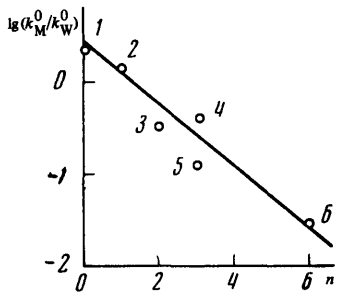


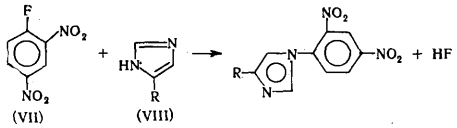
Figure 6. Dependence of logarithm of ratio of rate constants in micellar k^0_M and aqueous k^0_W phases for the acylation of m-bromobenzaldehyde oxime on number n of methyl and methylene groups in acyl portion of p-nitrophenyl carboxylate acylating agent: 1) salicylate; 2) acetate; 3) β-phenylpropionate; 4) $\alpha\alpha$-dimethylpropionate; 5) butyrate; 6) heptanoate[4].

A semi-quantitative interpretation of this effect is that ions and aromatic molecules are sorbed in the surface layer of the quaternary ammonium micelles, whereas the aliphatic chains on solubilisation by the micelle are immersed in the hydrophobic core. Thus increase in size of the aliphatic portion R will secure an orientation of the ester molecule such that both R and the ester group will be drawn into the hydrophobic core of the micelle. This, of course, would prevent its interaction with the oxime ion. It may be postulated as a first approximation that every methyl or methylene group makes a roughly constant positive contribution, equal to the incremental free energy of transfer of this group from the hydrophobic core to the hydrated surface layer, to the free energy of activation of the reaction in the micellar phase. The validity of such a view is indicated by the linear relation between $\lg(k^0_M/k^0_W)$ and the number n of methyl and methylene groups in the radical R (Fig. 6), whose slope gives +0.43 kcal $mole^{-1}$ (for each methylene or methyl group) as the increment in the free energy of transfer.

This phenomenon is remarkable in indicating the possibility of specificity in micellar catalysis. Indeed this is a case not of "trivial" specificity due to the concentration effect (the stronger the binding the greater the acceleration) but of finer "tuning" of the catalyst, when substantially different acceleration effects are obtained with similarly bound substrates.

The situation with regard to research on micellar catalysis in bimolecular reactions involving only uncharged molecules is far worse, although this particular case is far easier to analyse theoretically because of the absence of effects due to variation of the surface potential. A reaction of this type—between fluoro-2,4-dinitrobenzene

(VII) and the methyl ester of *N*-benzoyl-L-histidine (VIII) [sic]



(46)

has been used[71] to solve the important problem of activation energy in micellar catalysis. "Experimental" values E_{exp}, obtained from the temperature dependence at some constant value of C

$$E_{exp} = -R\left(\frac{\partial \ln k_{exp}}{\partial (1/T)}\right)_C \qquad (47)$$

have normally been employed. However, this quantity is equal to the true activation energy of the reaction occurring in the micellar phase only for a unimolecular reaction, provided that limiting values of k_{exp} are used at sufficiently large values of C. In all other cases E_{exp} is composite (as will be shown below), and therefore its value must be interpreted with caution. From the decrease in E_{exp} in the presence of hexadecyltrimethylammonium bromide, which catalyses the alkaline hydrolysis of chloro-2,4-dinitrobenzene, and its increase when the same reaction was inhibited in the presence of sodium dodecyl sulphate, it was concluded[37] that the transition state of the reaction is stabilised by the surface charge of the micelle during catalysis, and destabilised during inhibition. However, it is then difficult to explain why E_{exp} passes through a minimum with increase in C in the catalysis of the alkaline hydrolysis of fluoro-2,4-dinitrobenzene by the quaternary bromide[38], whereas it increases with increase in C during micellar catalysis of the alkaline hydrolysis of *p*-nitrophenyl diphenyl phosphate[82]. Similarly, the lower value of E_{exp} for the acid hydrolysis of sodium dodecyl sulphate as compared with that of sodium ethyl sulphate led to the conclusion that the transition state is stabilised by the anionic micelle of this surfactant (whose rate of hydrolysis exceeds that of sodium ethyl sulphate by a factor of 60)[83]. But it then remains obscure why the acid hydrolysis of the surfactant is characterised by the same value of E_{exp} before and after the c.m.c.[84] Yet all these facts can be explained perfectly satisfactorily by using the above simple concepts of the approach or separation of ionic and hydrophobic reactants. From Eqn. (21) with $\bar{k}_M K_A K_B C \gg k_W$ and Eqn. (47) it follows that

$$E_{exp} = E_M + \frac{\Delta H_A}{1 + K_A C} + \frac{\Delta H_B}{1 + K_B C} \cdot \qquad (48)$$

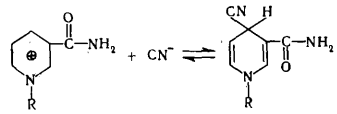
The composite quantity E_{exp} is seen to include also the heats of binding of the reactants by the micelles and to depend on C. For reaction (46) between uncharged reactants it was found that $E_M \simeq E_W$, and the very considerable decrease in E_{exp} observed is due to negative heats of binding of the reactants[71].

The binding by micelles of reactants containing no charged groups is due mainly to hydrophobic interactions. Therefore cation-active, anion-active, and non-ionic surfactants should act as catalysts, with the action of ionic surfactants unaffected by the concentration of the gegenions. This occurs in the case of reaction (46),[71] and also for the reaction of aniline with chloro-2,4-dinitrobenzene or fluoro-2,4-dinitrobenzene[85].

However, very considerable specific electrostatic effects are nevertheless possible in the micellar catalysis of reactions between uncharged molecules. An example is the reaction of (VIII) or other imidazole derivative with *p*-nitrophenyl carboxylates[71]. These reactions are accelerated by hexadecyltrimethylammonium bromide, retarded by sodium dodecyl sulphate, and slightly dependent on the concentration of a non-ionic surfactant. Catalysis by the quaternary bromide is sharply depressed in the presence of gegenions. At the present time it is difficult to establish whether these effects are due to orientation of the reactant in the micelle or are a direct effect of the surface charge of the micelle on the transition state of the reaction. In any case, the presence of such effects indicates the existence of extremely untrivial ways in which surfactant micelles influence the kinetics of organic reactions.

V. EFFECT OF MICELLES ON REACTION EQUILIBRIUM

The influence of micelles on ionic equilibria is well known. The effect of surfactant micelles has been most fully studied on the dissociation constants of acids and bases[2,23]. The shift in pK_a produced by ionic surfactants can in general be satisfactorily described on simple electrostatic concepts, of the type applied by us to the kinetics of ion–molecule reactions. The shift usually reaches 1–2[2,23], corresponding to the observed 10–100-fold acceleration of such reactions. The most considerable changes in ionic equilibrium constants have probably been found in the reaction



(49)

where the equilibrium constant increases by a factor of 25 000 in the presence of hexadecyltrimethylammonium bromide[86].

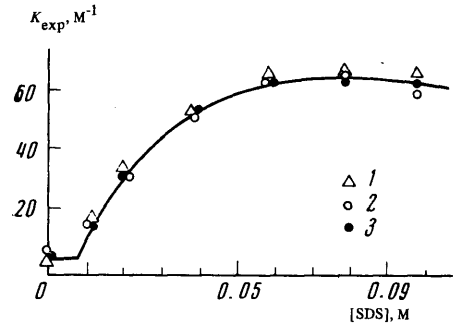


Figure 7. Effect of sodium dodecyl sulphate on experimental equilibrium constant for the formation of benzylideneaniline: 1) values calculated from equilibrium concentration of benzylideneaniline; 2) ratios of rate constants of forward and reverse reactions at pH 7; 3) ratios at pH 10.[8]

An example of the displacement of a non-ionic equilibrium[8] is the effect of sodium dodecyl sulphate on the equilibrium constant of the formation of benzylideneaniline by reaction (41). Fig. 7 illustrates the dependence of the experimental equilibrium constant on the surfactant concentration. These results were discussed on the basis of

a rapidly established distribution of reactants between aqueous and micellar phases. The experimental equilibrium constant

$$K_{exp} = \frac{[AB]_0}{[A]_0[B]_0} \quad (50)$$

is then related[8] to the surfactant concentration by the formula

$$K_{exp} = K_W \frac{1 + K_{AB}C}{(1 + K_A C)(1 + K_B C)} \quad (51)$$

where K_A, K_B, and K_{AB} are binding constants of the reactants with the micelles and K_W is the equilibrium constant in water. The true equilibrium constant in the micellar phase is

$$K_M = \frac{[AB]_M}{[A]_M[B]_M} = \frac{[AB]_0}{[A]_W[B]_W} \cdot \frac{P_{AB}}{P_A P_B} = K_W \frac{P_{AB}}{P_A P_B}. \quad (52)$$

The binding constants of the reactants with the surfactant micelles were found from Eqn. (51) by analysing the dependence of K_{exp} on C (Fig. 7). The results were almost identical with independent measurements using the gel filtration of the reactants in an aqueous solution of the surfactant[8]. This demonstrates the validity of the theoretical equation (51). Moreover, it was found that $K_M \leqslant K_W$. Despite a more than tenfold increase in the experimental equilibrium constant K_{exp} (Fig. 7), the true equilibrium constant in the micellar phase K_M is thus roughly equal to K_W (or even less). This phenomenon is directly analogous to the acceleration of reactions by the localisation of the reactants.

In view of these facts the term "micellar catalysis" is not entirely correct, since a "true" catalyst should not displace an equilibrium appreciably[87]. Nevertheless, this term has become established and is a quite happy choice, for it reflects the facts firstly that a surfactant has a substantial effect on reaction velocities when added in low concentrations ($\leqslant$0.01 M) and secondly that the surfactant is not used up in the reaction.

ADDENDUM

A considerable number of studies of micellar effects in various organic reactions have been published since the appearance of the review[2]. Some of them are covered in the present Review (see above), but several investigations, not specially concerned with physicochemical aspects, have not been mentioned. Among them we may note the following—alkaline decolorisation of triphenylmethane dyes[88-90], hydrolysis of carboxylic esters[91-93] and ethers[94], hydrolysis and aminolysis of phenyl sulphates[95], acylation of thiols[96], interaction of the hydroxide ion with tetranitromethane[97] and of the cyanide ion with 3-carbamoylpyridinium ions[98], azo-coupling[99], deamination of amines[100] and hydroxylamines[101], decarboxylation[102], addition of cyanide to haemin[103], reactions of Cl_2^- and hydroxyl radicals[104,105], activation of complex ions[106], and other reactions[107,108]. Catalysis by "reversed" micelles in non-aqueous solvents is especially interesting. The mutarotation of 2,3,4,6-tetramethyl-α-D-glucose in benzene and in cyclohexane[109], the aquation of complex ions in benzene[110], and other reactions[111-113] have been studied in such systems.

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Department of Chemical Kinetics,
Lomonosov Moscow State University

U.D.C. 541.113;541.135

Heat Capacity of Aqueous Solutions of Electrolytes

V.A.Latysheva

The present review deals with studies of the heat capacity of aqueous solutions of electrolytes. The material has been selected to show the extent to which the studies which have been carried out reveal the relationship between the heat capacity of the solutions and their internal chemical character, with reference to the dependence of the heat capacity of solutions on their structure, the hydration and hydrolysis of ions, the formation of acido-complexes, etc. Some promising possibilities provided by the study of the heat capacity of aqueous solutions of electrolytes have been noted. The bibliography contains 264 references.

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I. INTRODUCTION

The study of the heat capacity of aqueous solutions of electrolytes is being initiated in various spheres of theoretical and practical research. In the period 1960–1971, heat capacity was studied in connection with the development of efficient adsorption refrigerating machines [1], the technology of wet spinning [2], methods of distilling and processing sea water [3–8], and the rationalisation of the production of alumina [9–17] and other materials [18–28]. In most of the works cited, narrow problems of a practical character were resolved, but an incomparably greater number of studies were aimed at determining the relationship between heat capacity and the nature of solutions. This tendency is natural, since the search for general regular features, directed in the final analysis towards the development of a theory of solutions, should be much more effective than utilitarian studies in leading to the rapid elimination of the marked inadequacy of data on the heat capacity of solutions, which makes itself felt everywhere—from the non-ferrous metal industry [29] to the study of the functions of nucleic acids [30].

II. SOME THEORETICAL IDEAS

Essentially no development of fundamentally new theories of the heat capacity of solutions has taken place in recent years. We can only say that attempts have been made to develop, verify, or discuss the theoretical ideas previously put forward by Born [31] and Webb [32], Everett and Wynne-Jones [33], Everett and Coulson [34], Eley [35], Frank and Evans [36], Frank and Wen [37], Eucken [38–40], Kapustinskii [41,42], and others.

The application of the Born–Webb theory invariably encounters difficulties, associated with the fact that this theory does not take account of the molecular nature of the solvent [35,43–48]. Thus for example it has been shown convincingly [43,44] that the equation for the dependence of the partial molar heat capacity of ions at infinite dilution $\overline{C}^0_{p_2}$ on the radius of the ion:

$$\overline{C}^0_{p_2} = f_1\left(\frac{e^2}{r}\right) + f_2(e) \qquad (1)$$

where e is the charge and r the radius of the ion, derived by Kapustinskii [41,42] using only the Born equation, does not show even qualitative agreement with experiment. The slope of the theoretical curve is the opposite of that observed experimentally. Agreement with experiment can be obtained only by taking account of "the effect of the long-range action of ions on water, which should be negative and should increase with increase in the ionic radius and with increase in the complexity of the configuration of the ion" [43]. Eqn.(1) should then be replaced by:

$$\overline{C}^0_{p_2} = f_1\left(\frac{e}{r}\right)^2 + f_2(e) + f_3(r\varkappa), \qquad (2)$$

where $\varkappa$ is a coefficient characterising the configuration of the ion.

At the present time the Born–Webb theory is sometimes used only as a means of estimating the electrostatic components of the thermodynamic characteristics of ions in solution. The use of this method in practice is based on the need to know the effective dielectric constant of water in solutions, and its derivatives with respect to temperature. Thus some authors start from the converse;

they use some independent method of estimate these electrostatic components, and then calculate the effective dielectric constant and its derivatives[49]. In the case of heat capacity, compressibility, and thermal expansion, however, the attempts to carry out these estimates appear unsuccessful, partly because of the lack of accurate data[49], but chiefly because of the complexity of the interpretation of these properties[45,46]. The significant correction which was introduced into the electrostatic theory by Everett and Coulson[34] and which takes account of the unique state of the water molecules closest to the ion, did not lead to agreement with experiment[34,45]. Conway and coworkers[45] showed that the change in heat capacity ΔC associated with the effect of the restriction of the liberations of the water molecules closest to the ion is relatively small in magnitude and has the same sign as the change in entropy ΔS in the corresponding process, and that ΔC and ΔS should change in the same sense on going from one system to another. At the same time the order of change in the values of $\overline{C}_i^0$ for the ions of the alkali and alkaline earth metals and the halogens, and also the values of ΔC_V (the changes in heat capacity at constant volume) for the ionisation of methylammonium ions, obtained from the experimental data, are opposite to the corresponding orders for $\overline{S}_i^0$ and ΔS, and the signs of the quantities $\overline{C}_i^0$ and ΔC may be the opposite of the signs of $\overline{S}_i^0$ and ΔS (Fig.1). On this basis, Conway and coworkers[45] exclude the effect indicated by Everett and Coulson from the factors determining the magnitude of $\overline{C}_{pi}^0$ and give preference to the influence of ions on the structure of water. They assume that the positive values of $\overline{C}_{pi}^0$ for cations and the negative values for anions may be due to the structure-forming influence of cations and the destructive influence of anions.

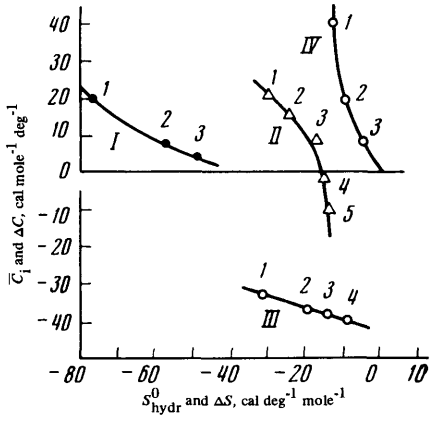


Figure 1. Comparison of the partial g-ion heat capacity of monatomic ions $\overline{C}_i$ (curves *I*–*III*) and the change in heat capacity in the protolytic dissociation of alkylammonium ions ΔC (curve *IV*) respectively with the entropy of hydration of the monatomic ions S^0_{hydr} and the change in entropy ΔS in the protolytic dissociation: *I*) Mg^{2+} (*1*), Ca^{2+} (*2*), Ba^{2+} (*3*); *II*) Li^+ (*1*), Na^+ (*2*), K^+ (*3*), Rb^+ (*4*), Cs^+ (*5*); *III*) F^- (*1*), Cl^- (*2*), Br^- (*3*), I^- (*4*); *IV*) $(CH_3)_3NH^+$ (*1*), $(CH_3)_2NH_2^+$ (*2*), $(CH_3)NH_3^+$ (*3*).

It should however be noted that Conway and coworkers use the values of $\overline{C}_{pi}^0$ on Eucken's scale, without justifying its use in preference to other scales. It is quite possible that scales in which the values of $\overline{C}_{pi}^0$ for cations are not positive but negative will prove more correct (this will be discussed later). Moreover, the changes in the opposite sense noted by the authors cited for $\Delta\overline{S}_i^0$ and $\overline{C}_{pi}^0$ may indicate merely that the effect of partial freezing of the degrees of freedom of the water on hydration overlaps the effect of change in structure, but not complete absence of the first effect.

In order to reveal the existence of the first effect, it is necessary to compare the heat capacities of ions not within the vertical groups of the periodic system but along the horizontal periods of elements with similar steric and electrostatic parameters (*d* or *f* elements). This approach has been made by a number of authors[50-55]. Study of the heat capacity of aqueous solutions of the perchlorates of the 3*d* metals (Mn^{II}, Co^{II}, Ni^{II}, Cu^{II}, and Zn) showed that the values of $\overline{C}_p^0$ for these electrolytes, on going from one ion to another, change in the same sense as the values of ΔH, ΔG, and ΔS for the hydration of the cations (Fig. 2).[50-53] Thus the strength of binding of water by the ions still has significant importance for the heat capacity. The study of the heat capacity of solutions of salts of the rare earth elements led to similar conclusions[54,55]. The concept of the influence of ions on the structure of water has attracted the greatest attention from research workers[35-37,56-58]. In particular, the ideas of Frank and coworkers[37] on the cluster structure of water and solutions have provided the basis for several recent theoretical and experimental studies[59-70]. Nemethy and Scheraga[59] suggest that the water molecules inside the clusters, on the surface, and outside the clusters differ from one another in the number of hydrogen bonds which they form and in the changes which they bring about in the vibrational spectrum of water. On the basis of this premise, Nemethy and Scheraga developed a statistical method for calculating the concentration and size of the water clusters and the thermodynamic properties of water from data on the vibrational spectra. The calculations do not show complete agreement with experiment for pure water (the method has not been used for aqueous solutions of electrolytes); in the opinion of Vand and Senior[60], this is due to underestimating the number of straight and branched chains in the structure of water. Attempts have been made to develop a theory of aqueous solutions of electrolytes from the semi-empirical theory of Eucken[38-40,71,72], based on the view that in solutions an equilibrium is established between monomers, dimers, tetramers, and octamers of water molecules and hydrated ions. Wicke compared new experimental data on the heat capacity of aqueous solutions of a number of alkali metal halides, alkylammonium salts, and aliphatic acids and their salts at temperatures in the range 0–130°[61,73] with the results of studies of other properties of the solutions carried out by different authors, and concluded that Eucken's theory is inadequate and that it is necessary to take into account the existence, in water and aqueous solutions, of structural units of the "flickering cluster" type, in Frank's terminology[37]. However, in the opinion of Wicke (and many others[46,61,74-76]) Frank's two-structure model is inadequate for a satisfactory description of the heat capacities of solutions. Wicke puts forward the so-called combined model of the structure of water, which as it were combines elements of the models of Eucken and Frank.

On the basis of this model, Wicke[61] and Rueterjans and coworkers[69] put forward an explanation of the form of the

temperature dependence of $\bar{C}_p^0$ for a number of simple halides (the existence of a maximum at temperatures in the range 50–90°) and the characteristic features of the heat capacity of solutions of tetra-alkylammonium halides ($\Phi C > 0$).

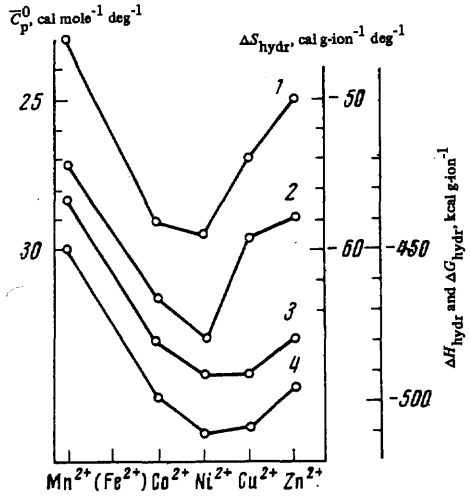


Figure 2. Comparison of the values of $\bar{C}_p^0$ for the perchlorates of the 3*d* metals (*1*) with the entropy ΔS_{hydr} (*2*), free energy ΔG_{hydr} (*3*), and enthalpy ΔH_{hydr} (*4*) of hydration of the corresponding cations.

The theoretical studies of Lovett and Ben-Naim [77], devoted to solutions of the inert gases in water, have proved of interest in the elucidation of the nature of the structure-forming influence of the non-polar parts of electrolytes on water. The one-dimensional model of aqueous solutions of the inert gases put forward in the work cited, and statistical calculations using this model, lead to the unambiguous conclusion that the introduction of inert gas molecules into heavy water (D_2O) should lead to less stabilisation of the structure than their introduction into ordinary water (which is less structured than heavy water). This difference is in fact observed and is based on the fact that (according to the model) the inert gas can stabilise the structure only when the water contains open cavities into which the gas can penetrate. The less structured water has more of these cavities.

Krestov and coworkers [78,79] approached the problem of heat capacity from the viewpoint of the theory of positive and negative hydration, developed by Samoilov [80]. Like Noyes [49], Krestov and coworkers [79] assume that the change in heat capacity accompanying the hydration of ions ΔC_phydr can be broken down into two parts, one of which, ΔC_{pI}, is not related to the electrostatic parameters of the ion and is equal to the effect of the hydration of an inert gas atom having the same radius as the ion, whereas the other, ΔC_{pII}, depends on the nature of the effect of the electrostatic field of the ion on the structure of the surrounding water. Arguing within the framework of Samoilov's theory, the authors cited represent the quantity ΔC_{pII} as resulting from the partial compensation of two effects of the influence of ions on water: 1) the orientation of the nearest molecules in the field of the ion, and 2) the breakdown of the bonds between further-removed water molecules. The first effect should be accompanied by a decrease in heat capacity as a consequence of the decreased mobility of the molecules, and the second should be accompanied by an increase, since the water molecules become more mobile. Since the first effect predominates for ions with positive hydration, and the second effect predominates for ions with negative hydration, it is to be expected that for the former $\Delta C_{pII} < 0$, whereas for the latter $\Delta C_{pII} > 0$. The results of calculations carried out by Krestov and Klopov [79] confirm these suggestions, but they contradict the widely held opinion that the rupture of bonds in the structure of water should lead not to an increase in heat capacity but to a decrease; this is confirmed by the experimentally observed decrease in the values of $\bar{C}_p^0$ for alkali and alkaline earth metal salts and for the halides of the sub-groups with increase in the size of the ions [43,81]. On examination it was found that the contradiction was due to errors in the calculation of ΔC_{pI}, [79] carried out using data on the solubility of the inert gases in water [82]. The correct calculation leads to positive values of ΔC_{pI}, which within the limits of error are the same for all the inert gases (~40 cal mole^{-1} deg^{-1}) and to values of $\Delta C_{pII\,corr}$ which in all cases are negative and decrease with increase in the size of the ions in the sub-groups (column 4 of Table 1).

Table 1. Values of ΔC_{pI} and ΔC_{pII} for various ions (cal g-ion^{-1} deg^{-1}).

Ion	ΔC_{pI} [79]	ΔC_{pII} [79]	$\Delta C_{pII\,corr}$ (for $\Delta C_{pI} = 40$)
Li^+	—4.8	—3.7	—48.5
Na^+	—17.8	+4.1	—53.7
K^+	—25.2	+5.8	—59.4
Rb^+	—35.0	+14.8	—60.2
Cs^+	—48.6	+27.6	—60.8
Mg^{2+}	—18.4	—23.5	—81.9
Ca^{2+}	—25.6	—18.1	—83.7
Sr^{2+}	—39.6	—8.0	—87.6
Ba^{2+}	—49.2	—1.7	—90.9
F^-	—15.2	—3.3	—58.5
Cl^-	—23.6	+4.8	—58.8
Br^-	—37.8	+17.6	—60.2
I^-	—47.9	+27.1	—60.8

If in addition we take account of the tendency, noted by some authors (see, for example, Ref. 82), for ΔC_p to increase from He to Xe, we obtained an even greater decrease in ΔC_{pII} with increased size of the ions in each sub-group.

This result confirms the view [43,83] that Samoilov's theory does not provide an understanding of the heat capacity of solutions, since "the thermostatics of solutions is related not to fluctuations in the structure, produced by the translational movements of the molecules, but to the average statistical characteristics of the systems".

The results of theoretical studies of the influence of the concentration of an electrolyte on $\bar{C}_p^0$ (in the range of medium and high concentrations) have been published by Mikulin (p. 44 of Ref. 23). In Mikulin's opinion, the nature of the dependence of the partial molar heat capacity of the electrolyte on concentration in concentrated solutions is determined by the form of the concentration dependence of the so-called electrostatic component of the free energy of the solution G^{el}. The latter is related to "the nature and magnitude of the electrostatic forces" (the interaction of the ions and the polarisation of the water molecules) which

lead to the formation of the "ionic atmosphere" and bring about a change in the properties of the solvent close to the ion" (p. 49 of Ref. 23). It has the form:

$$G^{el} = -RTm(a + b\sqrt{c}) \quad (3)$$

where C is the molarity of the electrolyte, and a and b are constants which are characteristic of each electrolyte and which depend on temperature and pressure.

An extremely interesting feature of Mikulin's approach is the model of the hydrated ion, which takes account of the possibility that around the primary hydrated ion there is a layer of water molecules for which the dielectric constant value is greater than that for pure water (p. 126 of Ref. 23). The magnitude of the increase in the dielectric constant of this layer depends on the individual nature of the ions, and this is responsible for the specific character of the values of a and b in the equation for concentrated solutions. This unique layer is limited to a distance of 10–12 Å from the centre of the ion, so that in the range of highly dilute solutions it does not determine the form of the concentration dependence of G^{el}, which becomes the same for all electrolytes of the same valency type, in accordance with the Debye–Hückel theory.

Mikulin's theory has been critically reviewed[43]. The work cited also summarises the theoretical ideas previously developed by Mishchenko and coworkers on the factors determining the concentration and temperature dependence of the partial molar heat capacities of water and electrolytes in solution.

Drakin and coworkers[84] suggested that there is a linear relationship between the heat capacity of the hydration of ions ΔC_h on the one hand and the charge of the ion z and its hydrate coordination number n on the other

$$\Delta C_h = -Azn, \quad (4)$$

where A is a proportionality coefficient, the magnitude of which is determined empirically, and ΔC_h is the difference between the partial molar heat capacity of the ion at infinite dilution and the heat capacity of the ion in a vacuum.

This dependence is based on the idea that each of the n water molecules surrounding the ion can be bound by hydrogen bonds to two other molecules and hence can act as the starting point for a chain of hydrogen-bonded water molecules. The ion, which possesses a charge, will influence the vibrations of the chain. The total effect of the ion should be proportional to nz. This idea is attractive for its simplicity, and at first sight it might seem to provide a basis for a new method for determining the coordination numbers of ions in solution. As shown below, however, not all of the ions studied by these authors[84-87] obey this relationship, and the authors themselves conclude that it is only approximate[87]. We doubt whether all the change in heat capacity when ions pass into solution can be attributed to the formation of the hydration sheaths of the ions.

The results of these theoretical studies show clearly that the heat capacity of solutions is sensitive to the most varied characteristics of the interaction between the components of solutions. Thus in order to develop a general theory it is necessary first of all to accumulate sufficiently extensive and reliable experimental data on the relationship between heat capacity and the various forms of interaction in solution, such as the hydration of ions, their association, their action on the structure of water, hydrolysis, complex formation, etc.

Data on the partial molar heat capacities of electrolytes in highly dilute solutions are of exceptional importance for the development of the theory.

III. THE PARTIAL MOLAR HEAT CAPACITIES OF ELECTROLYTES AT INFINITE DILUTION $\bar{C}^0_{p_2}$

1. Experimental Determination of $\bar{C}^0_{p_2}$

The values of $\bar{C}^0_{p_2}$ are usually determined by extrapolating the apparent molar heat capacities of the electrolyte ΦC_{p_2} to zero concentration. For this extrapolation to be successful, the experimental data on the specific heat capacity of the solutions c_p should be as accurate as possible[88].

In recent years there has been an increase in the number of laboratories in which precision heat capacity measurements are being made. There has been an increased number of materials for which accurate c_p values have been obtained for the first time or for which earlier inaccurate values have been accurately determined[84-87,89-128]. Only a few papers[106], however, cover the range of solutions with concentrations less than 0.1 m. This means that the values of $\bar{C}^0_{p_2}$ obtained by extrapolation are still unreliable, since at lower electrolyte concentrations a change in the slope of the plot of ΦC_{p_2} against $\sqrt{m}$ is still quite possible[43,51,53,87,113,118,119,122,129].

Parker[130] proposed a way out of situations of this kind; in this approach, the slope for very dilute solutions is calculated from the Debye–Hückel theory, after which the ordinate of the initial point of the calculated section is determined by assuming that the change from the calculated straight line to the experimental line should take place along the smoothest and shortest curve. This method was used to calculate $\bar{C}^0_p$ for a number of uni-univalent electrolytes, and also to estimate the heat capacities of various solutions of electrolytes which have been little studied (NH_4Br, NH_4I, RbI, and MX, where M = Rb or Cs, and X = OH, Cl, Br, or NO_3). The application of Parker's method to electrolytes of the 1:1 valency type, which are chemically relatively "simple", is apparently justified at present, but it can hardly be used in the case of electrolytes with highly charged ions, which often tend to undergo hydrolysis, or, by strongly polarising the nearest water molecules, bring about structural effects in dilute solutions, not taken into account by the Debye–Hückel theory. A number of authors who have carried out the precise determination of the heat capacity of aqueous solutions of the chlorides of the elements of the beryllium side group at 25°[90-94] suggest that $\bar{C}^0_{p_2}$ be determined by use of interpolation equations giving the concentration dependence of the specific heat capacity. This method has some advantages over graphical extrapolation, but it also is unreliable in the absence of data for dilute solutions.

Work devoted specifically to the question of the extrapolation of the values of ΦC_p to $m = 0$ [113] has shown that even such a relatively "simple" 1:1-valent electrolyte as NaI can show quite unexpected behaviour in the range of low concentrations.

The difficulties associated with the extrapolation of ΦC_{p_2} to $m = 0$ have led to the search for new methods of determining $\bar{C}^0_{p_2}$. One of these is known as the "method of integral heats", due to Cobble[131]. In this method, the values of $\bar{C}^0_{p_2}$ are determined from data on the heat capacity of an individual electrolyte C_{p_2} and the change in heat

capacity on dissolution ΔC^0_{pS}. The latter are found by differentiating, with respect to temperature, the first heats of dissolution of the electrolyte in water ΔH^0_S, found by extrapolating the integral heats of dissolution ΔH_S to zero concentration using the extended Debye–Hückel equation [132]. An advantage of this method is the greater reliability of the extrapolation of ΔH_S to $m = 0$ (m = molality) compared with the usual extrapolation of the apparent molar heat capacities of the electrolyte Φ_{C_2}, since the function which Criss and Cobble use in the extrapolation is linearly dependent on the molality. Nevertheless, even this extrapolation does not always give good results, as apparently indicated by the insufficiently "smooth" temperature dependence of ΔH^0_S, observed by these authors in a number of cases. The artificial smoothing of this dependence, undertaken by Criss and Cobble, is hardly justified for all systems, since the existence of an incompletely smooth temperature dependence for ΔH^0_S is apparently possible in principle (see p. 1779).

If in addition we take into account the unavoidability of error in the determination of the heat capacity of an individual electrolyte C_{p_2}, which sometimes reaches several cal mole^{-1} deg^{-1}, we can understand why the accuracy of the measured values of $\overline{C}^0_{p_2}$ obtained by Cobble's method in a number of cases differs little from that for the values of $\overline{C}^0_{p_2}$ obtained by extrapolating the Φ_{C_2} values (Table 2).

Table 2. Comparison of the values of $\overline{C}^0_{p_2}$ (cal mole^{-1} deg^{-1}) obtained by the method of integral heats (m.i.h.) and by measurement of the heat capacity of the solutions (m.h.c.s.). $t° = 25°$.

Electrolyte	$-\overline{C}^0_{p_2}$ (m.i.h.)	References	$-\overline{C}^0_{p_2}$ (m.h.c.s.)	References
HCl	30.5	96	29.2	88,138
			30.0	(pp.400 and 652 of Ref.132)
			32.6	139
NaCl	18.9	131	23.3	140
			21.6	141
$BaCl_2$	72.6	131	73.5	141
			73	142
			74.36	138
Na_2SO_4	46.7	101	50	140
CsI	36.6	98	31.02	42
			31.6	141

The method of integral heats is being used in many studies at the present time [65,68,69,95–103,121,126,133–137]. The lack of reliable data on the heat capacity of most individual electrolytes (particularly crystal hydrates), however, restricts the possibilities provided by the use of this method.

2. Semi-empirical Methods for Separating $\overline{C}^0_{p_2}$ into Ionic Components $\overline{C}^0_{p_i}$ and the Calculation of $\overline{C}^0_{p_i}$ for Different Temperatures

The problem of separating the heat capacity of an electrolyte into ionic components is even further from solution than the analogous problems of resolving into components the heats of hydration, volumes, and various other properties. There coexist ionic heat capacity scales which differ considerably from one another not only in the absolute values but also sometimes in the signs of the heat capacities [43,81]. In the resolution of heat capacities it may be necessary to use criteria different from those used in the separation of the enthalpy of hydration, since the heat capacity, which is the derivative of the enthalpy with respect to temperature, may be distributed between the ions in a way which is quite different from that for the actual integral heat [43]. The method of resolving the heat capacities proposed by Mishchenko and coworkers is based on the relationship between the heat capacities and the volumes of the solutions. The authors cited assumed that the values of $\overline{C}^0_p$ are equal for those ions for which Fajans and Johnson established that the partial molar volumes are equal, namely NH_4^+ and Cl^-. The scale of ionic heat capacities obtained on this basis is given in Table 3. Drakin and coworkers [84] suggested that the separation of $\overline{C}^0_{p_2}$ into ionic components be based on the assumption that $\overline{C}^0_{pCl^-} = -8$. [84] The authors cited obtained this quantity by selecting a value which would satisfy the equation (4) which they put forward for the relationship between the heat capacities and the hydration coordination numbers of ions.

Table 3. Values of $\overline{C}^0_{p_i}$ for various ions (cal mole^{-1} deg^{-1}) on different scales. $t° = 25°$.

Ions	Ref.43	Ref.143	Ref.145	Ref.81	Ref.130	Ref.146
H^+	−23.4	−3	−21	−20.5	0	+28
Li^+	−9.9	+12	−4.0	−8.0	+16.4	+41
Na^+	−15.0	+2	−9.9	−12	+11.1	+37
K^+	−21.6	−3	−17.5	−18	+5.2	+31
Rb^+	—	—	−20.3	−19	+3.3	+30
Cs^+	—	—	−22.7	−23	+1.9	+26
Be^{2+}	—	—	+16.3	−22	—	+76
Mg^{2+}	−51.3	—	−23.6	−36	—	+62
Ca^{2+}	−54.3	—	−39.5	−44	—	+54
Sr^{2+}	−57.0	—	−48.6	−46	—	+52
Ba^{2+}	−60.3	—	−54 4	−54	—	+44
F^-	+26.9	—	+3.6	−8	−25.5	−57
Cl^-	−6.6	−26	−11.8	−10	−32.6	−59
Br^-	−9.6	−26	−15.2	−12	−33.9	−61
I^-	−10.3	−27	−19.6	−13	−34.0	−62
NO_3^-	3.8	−15	—	−7	−20.7	−56
NH_4^+	−6.6	+12	—	—	+19.1	—
OH^-	−8.6	−29	—	−8	−35.5	−57

De Ligny and coworkers [143] put forward an original method for finding the heat capacity for the individual hydrogen ion, involving the determination of ΔC_p for the hydration of the H^+ ion from the cycle:

$$\begin{array}{ccc} H^+(aq) + Foc(aq) & \rightarrow & Fic^+(aq) \rightarrow {}^1/_2 H_2(gas) \\ \uparrow 4 & & \downarrow 2 \\ H^+(gas) + Foc(gas) & \leftarrow 3 & Fic^+(gas) \rightarrow H^+(gas) + \bar{e}(gas) \end{array} \qquad (5)$$

where Fic^+ represents the ferrocinium ion $(C_5H_5)_2Fe^+$, and Foc represents ferrocene.

In the calculation of this cycle it is assumed that the heat capacity of the hydration ΔC_p hydr of large ions of the type Fic^+ ($r = 3.8$ Å) is additively made up of electrostatic and non-electrostatic components, so that the difference ΔC_p hydr $Fic^+ - \Delta C_p$ hydr Foc is equal to the electrostatic component of the hydration of Fic^+ and can be calculated

from the Born equation. The other quantities are determined rigorously. This gave $\Delta C_{hydr\,H^+} = -8 \pm 8$ and $\overline{C}^0_{p\,H^+(aq)} = -3 \pm 8$. The values of the heat capacities of other ions calculated on this basis are given in Table 3.

Latysheva[81] proposes a method for estimating ionic heat capacities which is based on the analysis of vibrational spectra of hydroxonium and hydroxyl ions in aqueous solutions. The results of such an analysis have shown that the nature of motion of particles in hydrate shells, and also the characteristics of hydration of H_3O^+ and OH^- ions, are very similar[144]. Latysheva therefore assumes that $\overline{C}^0_{p\,H_3O^+}$ will differ from $C_{p\,OH}$ only by an amount equal to the difference between the internal specific heats of non-hydrated ions, and separates $\overline{C}^0_{p_2}$ into ionic components. The starting values of $C^0_{p_2}$ are taken from the work of Criss and Cobble[146]. The resulting scale is shown in Table 3.

In papers by Cobble[146,147], Naumov and coworkers[148-152], and Krestov and coworkers[135,145,153], the question of the separation of $\overline{C}^0_{p_2}$ into ionic components is examined at the same time as, and in relation to, the temperature dependence of the entropies and heat capacities of ions.

Criss and Cobble[146,147] took as a basis the possibility of calculating rigorously the mean partial molar heat capacity of an electrolyte $\overline{C}^0_{p_2}]_{t_1}^{t_2}$ in the temperature range t_1-t_2 using the thermodynamic relationship

$$\overline{C}^0_p|^{t_2}_{t_1} = \frac{\overline{S}^0(t_2) - \overline{S}_0(t_1)}{\ln T_2/T_1}. \qquad (6)$$

The authors cited took account of the lack of the necessary experimental values of $S^0(t)$, and tried to establish a quantitative relationship between the values of $\overline{S}^0$ at different temperatures for individual groups of ions, classified according to structural type (simple or complex) and sign of charge (cations or anions). As a result, Criss and Cobble formulated the correspondence principle: "A standard state can be chosen at every temperature such that the partial molar entropies of one class of ions at this temperature are linearly related to the corresponding entropies at some reference temperature":

$$\overline{S}^0(t_2) = a(t_2) + b(t_2)\,\overline{S}^0(t_1) \qquad (7)$$

where $a(t_2)$ and $b(t_2)$ are empirical constants for a given class of ion†. By choice of standard state at each temperature is meant the specification of $\overline{S}^0$ for the hydrogen ion at this temperature. Having assumed that at 25° $S^0_{H^+} = -5.0$ e.u. (in accordance with published data), Criss and Cobble had to assume that at 60, 100, and 150° this quantity had the values −2.5, 2.0, and 6.5 e.u. respectively, otherwise the simple linear correspondence principle was not obtained.

The authors cited showed that with this choice of conditions, for simple ions, the principle applies with a range of ±0.5 cal mole^{-1} deg^{-1} up to 150°, and on this basis they assumed that extrapolation to 200° is possible. The use of the correspondence principle makes it possible to estimate, simply and rapidly, unknown entropies of electrolytes at different temperatures, and average heat capacities within the temperature ranges indicated. The values of the entropies and heat capacities of individual ions obtained by this calculation can hardly be the true values, however, since it has not been proved that the form of the correspondence principle is necessarily linear.

† It is obvious that the analytical form of the expression of the correspondence principle corresponds to one of Karapet'yants' comparative calculation methods.

It is therefore not accidential that the values of $\overline{C}^0_{p\,H^+}$ at 25°, obtained by differentiation of the curve giving the dependence of $\overline{S}^0_{H^+}$ on T and equal to 28 cal mole^{-1} deg^{-1}, and also the complete scale of ionic heat capacities based on this value by Criss and Cobble (see Table 3), have been criticised by a number of authors[81,135,153]. The high positive values of $\overline{C}^0_p$ for cations, and the large negative values of $\overline{C}^0_p$ for anions appear unjustified, if we take into account the more energetic binding, on the average, of water molecules by cations, and their larger hydration numbers. The increase in the values of $\overline{S}^0_{H^+}$ with increase in temperature also appears unnatural, since for a positively hydrated cation, such as the H^+ ion, the effect of the ordering of the structure when the ion is placed in water should predominate over the destructive influence to a still greater extent at higher temperatures[43].

Khodakovskii and coworkers[148-152] critically reviewed available published data on the equilibrium constants of processes involving the participation of different ions at different temperatures, calculated the heat capacities of many ions over a wide range of temperatures, and concluded that the temperature dependence of $\overline{C}^0_{p_2}$ is described satisfactorily by the equation

$$\overline{C}^0_{p_2} \cong bT. \qquad (8)$$

This approximation is applicable only for calculations in the temperature range 200−300°, that is at temperatures at which most of the hydrothermal processes in which these authors were interested took place, but it does not describe the extremal form of the dependence of $\overline{C}^0_{p_2}$ on $t°$ in the temperature range from 20° to 80°.[135] Having shown convincingly that the values of $\overline{S}^0_2$ obtained by Cobble and Criss are not absolute, the authors cited proposed new equations for the relationship between $\overline{C}^0_{p_2}$ and $\overline{S}^0_2$ for ions. These equations are not rigorous either, however, since they are based on the approximation $\overline{C}^0_{p_2} \simeq bT$ examined above.

An interesting attempt to obtain consistent values of the partial molar heat capacities and entropies of ions in infinitely dilute solutions in the temperature range 0−100° was described by Krestov and Kobenin[135,145,153]. On the basis of the concepts of the electrostatic and non-electrostatic contributions to the entropy and heat capacity of hydration of ions, developed by Krestov and coworkers[78,79,155-158], Krestov and Kobenin derived an equation for the partial molar entropy of the hydrated ion‡ at a temperature T, $S^T_{aq.i}$

$$\overline{S}^T_{aq\ i} = S^{298}_{aq\ i} + 45.7 \ln T/298 + \Delta a_T + \Delta b_T |z| + \Delta d_T \frac{|z|}{r_{aq}} \qquad (9)$$

and from this, by appropriate differentiation, they obtained the relationship

$$(C_p)^T_{aq\ i} = 45.7 + \left(\frac{\partial \Delta a_T}{\partial T} + \frac{\partial \Delta b_T}{\partial T}|z| + \frac{\partial \Delta d_T}{\partial T}\frac{|z|}{r_{aq}}\right) T \qquad (10)$$

where $S^{298}_{aq.i}$ and $(C_p)^T_{aq.i}$ are respectively the partial molar entropy at 298°K and the partial molar heat capacity at T for the ion in an infinitely dilute solution; z is the charge of the ion; r_{aq} is the radius of the hydrated ion, equal to $r_{crystallographic}$ + an increment q; and Δa_T, Δb_T, and Δd_T are constants at a temperature T.

‡ In the works cited, the quantities $\overline{C}^0_{pi}$ and $\overline{S}^0_i$ are meant, although the corresponding terms are not introduced in the text.

To determine the constant coefficients, the authors cited wrote Eqn. (10) in the form

$$(C_p)'^{T}_{aq\ i} = 45.7 + \left(\frac{\partial \Delta a_T}{\partial T} + \frac{\partial \Delta b_T}{\partial T}|z| + \frac{\partial \Delta d_T}{\partial T}\frac{|z|}{r_{aq}}\right)T - (C_p)'^{T}_{H^+\,aq}\ z \quad (11)$$

and solved the system of equations (11) for several ions. Here, $(C_p)'^{T}_{aq.i}$ is a conditional quantity which is smaller than the "absolute" heat capacity of the hydrated ion by the "absolute" heat capacity of the hydrated proton at the temperature T, multiplied by the charge of the ion. The $(C_p)'^{T}_{aq.i}$ values were determined from experimental data on the heat capacity of the hydrogen halides and other halides, with the condition that $(C_p)'^{T}_{aq.H^+} = 0$. By integrating the temperature dependence of the coefficients in Eqn. (11), the authors cited calculated Δa_T, Δb_T, Δd_T, and $S^T_{H^+}$ in the range 0–100°.

The values of $\overline{C}^0_{pi}$ for a large number of ions were obtained by this method [145]. Some of these values are given in Table 3. The values of $\overline{S}^0_{H^+aq}$ obtained by Cobble and by Krestov and Kobenin are compared in Table 4. It can be seen that with increase in temperature the values of $\overline{S}^0_{H^+}$ being compared change in opposite directions; there is a stronger physical justification for the direction of the change in $\overline{S}^0_{H^+}$ given by Krestov and Kobenin, so that more reliance can be placed on the value of $(C_p)^{298}_{H^+aq}$ obtained by Krestov and Kobenin. An interesting feature is that this value practically coincides with the corresponding value obtained by Latysheva [81] by a completely different method. The method of Krestov and Kobenin, unlike that of Cobble and Criss, does not require the artificial fixing of the values of $S^T_{H^+}$ at several temperatures, so that it appears more "absolute".

The only conditional quantity introduced into the calculation by Krestov and Kobenin is $\overline{S}^{298}_{H^+} = -2.1$ e.u. This method also, however, can only be regarded as approximate, since it is based on the assumption that the non-electrostatic components of the thermodynamic characteristics of the hydration of ions and inert gases are equal. This assumption is obviously incorrect for ions which are not of the noble gas type, as confirmed by the significant discrepancies between the calculated and experimental values of ΔC_p for the hydration of the chlorides of the rare earth elements (REE). [135]

In the case of ions of the noble gas type this assumption is of course more justified, but even in this case the calculation cannot be accurate, since it is known that a change in the charge of the nucleus can alter significantly the ratio of the electronic terms for the same number of electrons in the atom [159], and hence may influence the nature of the interaction of the ion with water.

To summarise, it may be stated that despite vigorous attempts to obtain real values of $\overline{C}^0_p$ for individual ions, this problem cannot yet be regarded as solved. The conditional scale of heat capacities ($\overline{C}^0_{pH^+} = 0$) therefore apparently has not lost its value completely, and it is still being used [43,130] (Table 3).

Table 4. Values of $\overline{S}^0_{H^+}$ at different temperatures.

t,°C	Ref.146	Ref.135	t,°C	Ref.146	Ref.135
25	−5.0	−2.1	100	+2.0	−6.0
60	−2.5	−4.3	150	+6.5	—

IV. THE RELATION OF THE HEAT CAPACITY OF SOLUTIONS TO THE VARIOUS TYPES OF REACTION OCCURRING IN THEM

1. Heat Capacity and the Hydration of Ions

The hydration of ions leads to changes in the state of not only the ions themselves and the nearest water molecules but also, in the great majority of cases, to a change in the structure of all the remaining water. The changes in heat capacity associated with the effects of the so-called short-range and long-range hydration may sometimes differ even in sign. In this connection, a number of papers emphasize one or other of these aspects of the phenomenon.

One of the most important characteristics of the short-range hydration of ions is the number of water molecules coordinated directly around the ion. Since the chemical binding of liquid water by salts on the formation of crystal hydrates [35,160] and even the covalent hydration of carbonyl groups [161] lead to a significant decrease in heat capacity, it was natural to expect the observation of a distinct relationship between the number of water molecules coordinated to the ions and the heat capacity of solutions. Attempts to find a quantitative relationship of this kind in analytical form were made by Drakin, Karapet'yants, and coworkers [84,86,87,122]. The relationship which they put foward was mentioned above [see Eqn. (4)]. To verify this equation, the heat capacities of aqueous solutions of a number of nitrates were studied. The values of n appearing in this equation for most cations were chosen on the basis of an analysis of the values of the coordination numbers in crystalline compounds of the corresponding elements [162,163] and for Cd^{2+} and Pb^{2+} by analogy with strontium and barium, in the same periods§. It was found that not all the ions are covered by this form of relationship. Apart all together from ions which do not have the inert gas structure, other ions such as Na^+ and Sr^{2+} are not covered. This may be due to insufficiently reliable estimation of the coordination numbers of the ions in solution and to the lack of justification for the view that the magnitude of the change in heat capacity on hydration is determined entirely by this single parameter. In actual fact, when the ions of elements belonging to different periods and sub-groups are compared, we can observe not only a change in the coordination numbers of the ions but also a change in the energy of the attachment of water molecules to the ions and in the extent to which ions influence the structure. The influence of the first of these factors was demonstrated in a study of the heat capacity of solutions of the perchlorates of the bivalent 3d elements, which have identical cation coordination numbers and similar structural parameters (see p. 1759). It is only for the ions of the REE, for which the structural similarity is even greater, that almost complete agreement is observed between the Φ_{C_p} values for their salts, if we consider the first and second halves of the REE series separately (Fig. 3). The difference between the Φ_{C_p} values for the two groups of elements in this case can in fact be attributed chiefly to the change in the coordination number of the cations [54,55]. The apparent absence of a correlation between the hydration energy of cations and the heat capacity of solutions in this case indicates the existence of some compensation effect, and

§ This analogy appears insufficiently justified in the case of Pb^{2+} and Ba^{2+}, in view of the marked difference in the electronic structure of these ions.

not that the heat capacity is independent of the binding energy of the water for the cations. This is possibly due to an intensification of the structure-forming action of the ions with increase in their field strength, particularly since the values of the standard entropy of the ions $\bar{S}_i^0$ decrease in the same direction, and in the alkali and alkaline earth metal series the action of the ions on the structure of water evidently becomes of primary importance (as already noted on p. 804).

Attempts have been made to consider heat capacity only in relation to structural changes. An original approach to the study of the influence of ions on the structure of water was made by Mrevlishvili and Privalov [164,165], who studied the temperature dependence of the heat capacity of frozen aqueous solutions of a number of electrolytes during heating, in order to estimate ΔS for the fusion of ice in the presence of various electrolytes. These values of ΔS differ significantly from the values of ΔS for the fusion of pure ice. In the opinion of the authors cited, this indicates a change in the structure of water under the influence of the ions. Thus for example it was found that Na^+ and Cl^- ions produce little change in the structure of water, whereas the K^+ ion destabilises it. The cations can be arranged in the following sequence of increasing ordering influence on water: $Mg^{2+} < Ca^{2+} < H^+ < Li^+ < Na^+$. A marked ordering influence on the structure is also shown by OH^- ions.

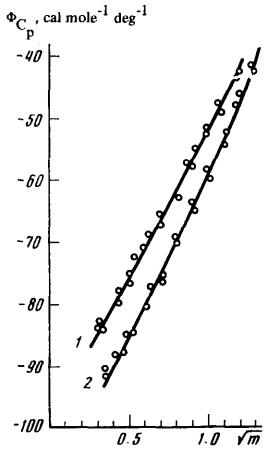


Figure 3. Dependence of ΦC_p for the chlorides of dysprosium, erbium, ytterbium (curve *1*), lanthanum, and neodymium (curve *2*) on the concentration of the solutions (m is the molality) at 25°. [54]

Papers by Mishchenko and coworkers, summarised in two reviews [43,116], emphasise the need to make simultaneous allowance for the binding of water in the hydrate sheaths of ions and the structural changes brought about in water, and examine the ratio of the contributions from these effects over a wide range of concentrations. In particular, it was shown that the role of structural changes is especially marked in dilute solutions and at low temperatures. At the same time the binding of water by ions becomes weaker at higher concentrations, as a consequence of the increase in the electrical viscosity in the solution, and this explains the increase in $\bar{C}_{p_2}^0$ with increase in concentration. In the region of the complete distribution boundary (CDB), a decrease in the energetic hydration of ions is possible, and this should lead to a further increase in $\bar{C}_{p_2}^0$. Further increase in concentration may be accompanied by a redistribution of the hydrate water in favour of the more hydrophilic partner. This should decrease the slope of the $\bar{C}_{p_2} = f(\sqrt{m})$ isotherm and may even lead to the production of a maximum. The possibility of the production of maxima in the range of "extremely high concentration" in the solutions was also predicted by Drakin and coworkers [166], who suggested that the production of maxima should be due to association in solution. In actual fact, maxima on the $\bar{C}_{p_2} = f(\sqrt{m})$ isotherms were observed for the salts of various REE. [54] Spedding and Jones attribute this to the possible formation of acido-complexes in concentrated solutions. In the section on heat capacity and complex formation it will be shown that this explanation is erroneous. The observation being discussed apparently corresponds more closely to the prediction of Mishchenko and coworkers.

The relative decrease in the role of the disruption of the water structure with increase in temperature and concentration was also demonstrated by Mashovets, Puchkov, and coworkers [9-17]. Mishchenko and Stagis were the first to study the heat capacity of solutions at the complete distribution boundary [167,168].

In an examination of the heat capacity of comparatively simple electrolytes (consisting of inorganic, generally monatomic, ions), only the breakdown of the intrinsic structure of water on the hydration of ions is discussed, whereas in the study of solutions of electrolytes including organic ions there is frequently encountered a phenomenon which is attributed to a strengthening of the intrinsic structure of water under the influence of the ions (see p. 805).

Ahluwalia and coworkers [65-67] determined the values of ΔC_p^0 of dissolution and $\bar{C}_{p_2}^0$ for a number of tetra-alkylammonium halides at 25° and 35°, and found that the ΔC_p^0 values increase in the order:

Me_4NI	$<$	Me_4NBr	$<$	Et_4NBr	$\simeq$	Et_4NI	$<$	Pr_4NBr	$\leqslant$	Pr_4NI	$<$	Bu_4NBr
-10.5 ± 6		-10.4 ± 4		33.0 ± 3		37.5 ± 4		112.5 ± 2		119 ± 4		179 ± 3

They conclude that Me_4N^+ cations break down the structure of water, and that the other cations strengthen it. The $C_p = f(T)$ and $\Delta C_p = f(T)$ curves are not monotonic [65] (Fig. 4). The minimum at 50° was explained in terms of "hydrophobic" interactions, and the maximum at 70° was explained on the assumption that the heat capacity of the structuring process decreases above 70°. The idea that large ions have a structuring action was confirmed by Boyd and coworkers [68], who studied the values of ΔC_p^0 for ion exchange by examining the temperature dependence of the values of ΔH^0 for the exchange of Na^+ and Bu_4N^+ on ion exchange resins.

Kresheck [169] determined $\bar{C}_p^0$ values for several amino-acids in infinitely dilute aqueous and heavy-water solutions at 25° and concluded that the non-polar side chains of methionine and norvaline promote structure formation in water, the effect being greater for light water than for heavy water, in agreement with the theoretical predictions of Lovett and Ben-Naim [77] (see p. 805). Kay and coworkers [62,63] compared the results of the study of many properties (thermodynamic and transport properties) of aqueous and non-aqueous solutions at several temperatures in terms of the theory of Frank and Wen; this enabled Kay

to divide ions into three classes: electrostrictional structure-forming (Li^+, F^-, Ca^{2+}), hydrophobic structure-forming (Bu_4N^+, Ph_4B^-, etc.), and structure-destroying (Cs^+, I^-, Me_4N^+).[62] The ion classification made by Kay leaves open the question of the possibility of an increased heat capacity due to the hydration of hydrophilic ions of inorganic character. Moreover, the opinion has grown in the literature that the dissolution of these electrolytes in water is always accompanied by a decrease in heat capacity[43,170]. Recently, however, it was found[171-175] that the temperature coefficient of ΔH for the dissolution of manganese and zinc perchlorate crystal hydrates is positive over an appreciable range of concentration, that is the ΔC_p values for the dissolution of these salts are positive and not negative. It was suggested that this effect is due to the formation, around the aquo-cations, of associates of water molecules, joined by hydrogen bonds. The formation of associates depends on the nature of the ions and the state of water in the corresponding aquo-complexes, and on this basis suggestions have been put forward regarding the cases in which ΔC_p for the dissolution of an electrolyte may be greater than 0 or less than 0. In the work cited, attention was drawn to the existence of characteristic features in the properties of dilute solutions, which can be understood qualitatively by assuming that the effect of the structuring of water by many ions is particularly marked in highly dilute solutions.

The question of the unique behaviour of heat capacity in the range of very dilute solutions was also dealt with in papers by Mishchenko and Novoselova[107-109,113], and agrees with studies of other properties of dilute solutions[129,176,177].

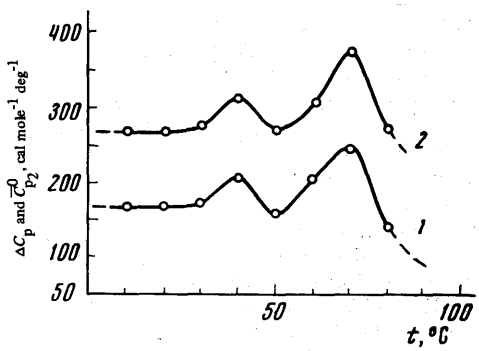


Figure 4. Temperature dependence of ΔC_p for the dissolution of tetraphenylborate in water (*1*) and $\overline{C}^0_{p_2}$ for tetraphenylborate (*2*).[65]

2. Heat Capacity and Hydrolysis of Ions

No special studies of heat capacity in relation to the hydrolysis of ions have been made in the period under review. It is possible only to try to estimate this effect from data on the change in heat capacity on the ionisation of water[178-180], ammonium ions and some of their derivatives[181,182], and acids[150,178,180-191], and also from the results of individual studies of the temperature dependence of the hydrolysis constants of metal cations[192-201].

Table 5 gives the values of ΔC_p for the ionisation of water for various acids and for the ammonium ion and its derivatives, obtained either as the temperature coefficients of ΔH for the reaction[178,180,181,186-188] or from the temperature dependence of the ionisation constants[150,181-185,190,191]. The values of ΔC_p for the hydrolysis of the anions formed on the dissolution of the uncharged acids listed in Table 5 are obviously equal to the difference between ΔC_p for the ionisation of water and ΔC_p for the protolytic dissociation of the acid. The corresponding values are given in column 5 of Table 5. It can be seen that the values of ΔC_p hydrol for the anions may be negative or positive.

Table 5. Values of ΔC_p for protolytic dissociation, ΔC_p p.d., for compounds, and values of ΔC_p for hydrolysis, ΔC_p hydrol, for the corresponding acid residues, at 25° (cal mole^{-1} deg^{-1}).

Proton donor	ΔC_p p.d.	References	Proton acceptor	ΔC_p hydrol
1	2	3	4	5
H_2O	−50 −52 −56.7	179 150 178	—	—
HNO_3	−36.9	150	NO_3^-	−13.1
HNO_2	−117	182, 183	NO_2^-	67
H_3PO_4	−37	181	$H_2PO_4^-$	−13
H_3PO_4	−43.5	150	$H_2PO_4^-$	−6.5
$H_2PO_4^-$	−54	181	HPO_4^{2-}	4
$H_2PO_4^-$	−49.7	150	HPO_4^{2-}	−0.3
HPO_4^{2-}	−169	150	PO_4^{3-}	119
H_3AsO_4	−37.2	150	$H_2AsO_4^-$	−12.8
$H_2AsO_4^-$	−65.6	150	$HAsO_4^{2-}$	15.6
$HAsO_4^{2-}$	−142	150	AsO_4^{3-}	92
H_2CO_3	−54.6	150	HCO_3^-	4.6
HCO_3^-	−54.6	150	CO_3^{2-}	4.6
H_2SO_3	−67.7	150	HSO_3^-	17.7
HSO_3^-	−68.5	150	SO_3^{2-}	18.5
HSO_4^-	−42.8	150	SO_4^{2-}	−7.2
$HSeO_4^-$	−99.3	150	SeO_4^{2-}	49.3
H_3BO_3	−460	150	$H_2BO_3^-$	410
H_4SiO_4	−35.3	150	$H_3SiO_4^-$	−14.7
$H_3SiO_4^-$	−135	150	$H_2SiO_4^{2-}$	85
H_4GeO_4	+686	150	$H_3GeO_4^-$	−736
H_6TeO_6	−13.9	150	$H_5TeO_6^-$	−36.1
$H_5TeO_6^-$	8.2	150	$H_4TeO_6^{2-}$	−58.2
HF	−28	150	F^-	−22
HCl	<0	191	Cl^-	>−50
H_2S	−68.5	150	HS^-	18.5
HS^-	−45	150	S^{2-}	−5
HCN	−36.2	185	CN^-	−13.8
HCN	−60	186	CN^-	10
CH_3COOH	−36	180	CH_3COO^-	−14
CH_3COOH	−34	187	CH_3COO^-	−16
$CH_2ClCOOH$	−36	187	CH_2ClCOO^-	−14
$CH_2BrCOOH$	−22	187	CH_2BrCOO^-	−28
CH_2ICOOH	−29	187	CH_2ICOO^-	−21
CH_2CNCO_2H (cyanoacetic)	−36	184	CH_2CNCOO^-	−14
$HO\cdot C_6H_4\cdot CO_2H$ (salicylic)	−45	188	$HOC_6H_4\cdot COO^-$	−5
$HOC_6H_4\cdot CO_2^-$	−33	188	$^-O\cdot C_6H_4CO_2^-$	−17
CH_3CHNH_2COOH (α-alanine)	−34	187	$CH_3CHNH_2CO_2^-$	−16
NH_2CH_2COOH (glycine)	−29 (−34.5)	187	$NH_2CH_2CO_2^-$	−21
$CH_3(CH_2)_2CH\cdot NH_2COOH$ (α-aminovaleric)	−30	187	$CH_3(CH_2)_2CH\cdot NH_2CO_2^-$	−20
NH_4^+	0	182	NH_3	—
$CH_3NH_3^+$	8; 7.5	181, 182	CH_3NH_2	—
$(CH_3)_2NH_2^+$	19.9	182	$(CH_3)_2NH$	—
$(CH_3)_3NH^+$	41.0	182	$(CH_3)_3N$	—
$OHNH_3$	−23	182	$OH\cdot NH_3$	—
$C_6H_5NH_3^+$	0.0	182	$C_6H_5NH_2$	—
$o\text{-}ClC_6H_4NH_3^+$	0.0	182	$o\text{-}ClC_6H_4NH_2$	—
(THAM) H^+	−17.4	178	THAM	—

The hydrolysis of metal cations involves essentially the protolytic dissociation of their aquo-complexes, so that subsequently we can try to estimate the values of ΔC_p for these processes by analysing the accumulated data for other acids.

Examination of the data in Table 5 reveals the following features.

1. The protolytic dissociation of uncharged molecules and anions is generally accompanied by a decrease in heat capacity, but the dissociation of positive ions almost always corresponds to an increase in heat capacity or to very little change.

2. The value of ΔC_p for the first stage of the dissociation of the uncharged molecules of many acids lies in the range between -22 cal mole^{-1} deg^{-1} and -38 cal mole^{-1} deg^{-1}. An exception is provided by acids which tend to decompose (HNO_2, H_2CO_3, H_2SO_3, H_2S) or polymerise (H_3BO_3, H_4GeO_4, H_6TeO_6), or which have a complex branched structure (THAM¶ or substituted carboxylic acids). It is also possible that some of these deviations are due to a large error in the determination of ΔC_p.

3. The value of ΔC_p for each successive stage of the step-wise dissociation of H_3PO_4, H_3AsO_4, and H_4SiO_4 is more negative than the previous one (Fig. 5).

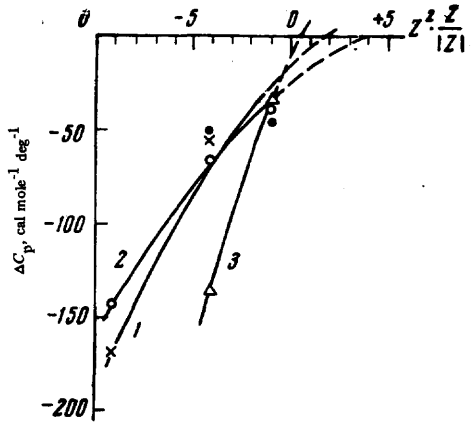


Figure 5. Values of ΔC_p for the successive stages of the acidic dissociation of H_3PO_4 (*1*), H_3AsO_4 (*2*), and H_4SiO_4 (*3*) as functions of the charge z of the conjugated base.

4. In the series of methylammonium ions, an increase in ΔC_p for the dissociation is observed with increase in the number of methyl groups.

The existence of several independent regular features, not to speak of the exceptions, indicates that the values of ΔC_p for the ionisation of protolytes are determined by various factors. One is the change in the electrostatic parameters of the particles in the dissociation process. This is obviously confirmed by the first three of the above regular features.

King [181] attempted to described ΔC_p for protolytic dissociation on the basis of Born's electrostatic model of hydration. He showed that, according to this model, ΔC_p for ionogenic reactions (corresponding to the dissociation of uncharged or anionic acids) should be negative, and should be more negative, the higher the charge of the anion. In the case of isoelectric reactions (for example the dissociation of NH_4^+), the absolute value of ΔC_p should be slightly greater, and possibly positive. Verification of the theory by experiment led King to the conclusion that the simple electrostatic model does not make it possible to predict ΔC_p quantitatively for protolytic dissociation [181]. It is necessary to take account of other factors influencing ΔC_p. Many authors consider that the most important of these factors is the hydration of the particles, including the rearrangement of the solvent as a result of the dissociation of the solute [180-184,186]. The temperature dependence of ΔC_p for the ionisation is particularly sensitive to these changes [180,182,184]. Thus if our aim is to estimate ΔC_p for the protolytic dissociation of the aquo-cations of metals

$$M(H_2O)_n^{z+} + H_2O \rightleftarrows MOH(H_2O)_{n-1}^{z-1} + H_3O^+$$

or in other words the hydrolysis of M_{aq}^{2+} cations, it is necessary to have not only the electrostatic parameters of the components of the reaction but also data (which are usually not available) on their hydration and action on the structure of the solution.

If we nevertheless assume that the electrostatic approach should be most applicable to metal ions of spherical shape, we may expect (following King's method [181]) for the hydrolysis of singly-charged metal ions ΔC_p close to zero, that for doubly-charged ions about 20–40 cal mole^{-1} deg^{-1}, and that for triply-charged ions 60–80 cal mole^{-1} deg^{-1}. It is difficult to verify this suggestion, since no direct calorimetric measurements of ΔC_p have been made. The known dependence of pK† for the hydrolysis of cations [192-201] on the reciprocal of the absolute temperature $1/T$ in most cases is linear, irrespective of the charge of the cation. Thus within the limits of error of the measurement of pK, the value of ΔC_p for the hydrolysis is equal to zero. The error in the measurement of pK, however, is nowhere less than ± 0.02 pK units; according to King's estimates [181], this would correspond to an error of several tens of cal mole^{-1} deg^{-1} in the determination of ΔC_p.

In a spectrophotometric study [191] of the hydrolysis of $FeCl_3$, $Fe(NO_3)_3$, and $Fe(ClO_4)_3$ it was found that ΔH for the reaction $Fe^{3+} + H_2O \rightleftarrows FeOH^{2+} + H^+$ in the temperature ranges from 21° to 50° and from 50° to 90° has the values 3.4 kcal mole^{-1} and 8.6 kcal mole^{-1} respectively. This gives the value $\Delta C_p \sim 150$ cal mole^{-1} deg^{-1}, which does not agree with the value -16.5 cal mole^{-1} deg^{-1} calculated on the basis of data on $\bar{C}_p^0$ for the components of the reaction, equal to -61 (Fe^{3+}), -39 ($FeOH^{2+}$), 18 (H_2O), and -20.5 (H^+) cal deg^{-1} mole^{-1}. [81]

From data on ΔS for the reaction $Al^{3+} + 2H_2O \rightleftarrows AlOH^{2+} + H_3O^+$, [201] the value of ΔC_p for this reaction can be estimated at about 30 cal mole^{-1} deg^{-1}. This value is also greater than the error in its determination, since it is found from the change in ΔS with temperature, which in this case is commensurate with the error in the determination of ΔS.

Thus the question of the values of ΔC_p for the hydrolysis of cations remains open. Nevertheless, it can hardly be assumed that the magnitude of this quantity has in fact the same zero value for all cations, since the state of the components of the solution changes quite markedly on

¶ THAM = tris(hydroxymethyl)aminomethane.

† $pK = \lg K$, where K is the hydrolysis constant.

hydrolysis and is different for different systems. This is indicated, for example, by the values of ΔS for hydrolytic processes, taken from a review by Arnek [202] (Table 6). The values of ΔS for the reactions of the same type involved in the formation of the complexes $CdOH^+$, $HgOH^+$, and $FeOH^{2+}$ vary from −2.7 e.u. to +23 e.u., those for complexes of the type $M_4(OH)_4^{4+}$ from −20.8 e.u. [for $Pb_4(OH)_4^{4+}$] to +14.0 e.u. [for $Ni_4(OH)_4^{4+}$], etc. It is difficult to believe that such marked differences in the entropy of the reaction are not associated with differences in the change in heat capacity. In actual fact, data on the measured heat capacity of aqueous solutions of the perchlorates of Mn^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+} at 25° [50,51,81,171] showed that in the range of high concentrations there is a correlation between the degree of hydrolysis of the cations and the apparent (and partial) molar heat capacity of the salts in solution (Fig. 6).

Table 6. Change in entropy ΔS accompanying the hydrolysis of cations $qM^{n+} + pH_2O \rightleftharpoons M_q(OH)_p^{(nq-p)+} + pH^+$ at 25° in 3 M $NaClO_4$. [202]

Hydrolysis product	ΔS, e.u.	Hydrolysis product	ΔS, e.u.	Hydrolysis product	ΔS, e.u.	Hydrolysis product	ΔS, e.u.
Be_2OH^+	0.2	$Fe_2(OH)_2^{4+}$	20.0	$CdOH^+$	−2.7	Hg_2OH^{3+}	−2.1
$Be_3(OH)_3^{3+}$	11.3	$Fe_3(OH)_4^{5+}$	22.0	Cd_2OH^{3+}	−5.1	$Hg_2(OH)_2^{2+}$	18.8
$(UO_2)_2(OH)_2^{2+}$	4.3	$Ni_4(OH)_4^{4+}$	14.0	$Cd_4(OH)_4^{4+}$	−9.4	$Pb_3(OH)_4^{2+}$	−15.8
$(UO_2)_3(OH)_5^+$	6.0	$Cu_2(OH)_2^{2+}$	4.4	$HgOH^+$	7.9	$Pb_4(OH)_4^{4+}$	−20.8
$FeOH^{2+}$	23.0			$Hg(OH)_2$	4.6	$Pb_6(OH)_8^{4+}$	−27.0

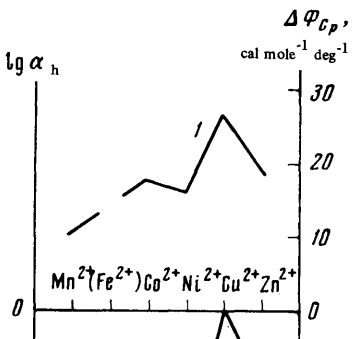


Figure 6. Correlation between the increase in the apparent molar heat capacity of the perchlorates of the 3*d* metals with increase in concentration from 0 to 4 *m*, $\Delta\Phi C_p$ (*1*) and the logarithm of the degree of hydrolysis $\lg\alpha_h$ for the corresponding cations in concentrated solutions of their chlorides (*2*).

If this correlation is not accidential, it indicates a positive change in heat capacity in the hydrolysis of these electrolytes in concentrated solutions. In the works cited it was suggested that a positive change in heat capacity may accompany the localised hydrolysis and hydrolytic polymerisation of cations, that is the processes which take place preferentially at high concentrations of the salt.

3. Heat Capacity and the Formation of Acido-complexes

The question of the change in heat capacity on the formation of acido-complexes in solution has been examined many times [7,10,11,54,203-228]. In all the works cited, with some exceptions [54,209,212-216,223,226], an indirect method for determining ΔC_p for complex formation from the temperature coefficients of the values of ΔH and ΔG was used. The main results are given in Table 7. It can be seen that the values of ΔC_p for ion association ΔC_{pk} vary over a wide range, depending on the specific ions, but are always positive.

Table 7. Change in heat capacity ΔC_{pk} on formation of various acido-complexes (cal $mole^{-1}$ deg^{-1}).

Process	T, °C	Ionic strength of medium I	ΔC_{pk}, cal $mole^{-1}deg^{-1}$	Reference
$Ni^{2+}+Suc^{2-}$ [a] $\rightleftarrows NiSuc$	0—45	0.1	42±20	203
$Co^{2+}+Suc^{2-} \rightleftarrows CoSuc$	0—45	0.1	72±20	203
$Mn^{2+}+Suc^{2-} \rightleftarrows MnSuc$	0—45	0.1	62±15	203
$Ni^{2+}+C_2O_4^{2-} \rightleftarrows NiC_2O_4$	0—45	supersaturated solutions	35±12	203
$Co^{2+}+C_2O_4^{2-} \rightleftarrows CoC_2O_4$	0—45	ditto	20±10	203
$Mn^{2+}+C_2O_4^{2-} \rightleftarrows MnC_2O_4$	0—45	»	65±5	203
$Co^{2+}+A^-$ [b] $\rightleftarrows CoA^+$	0—45	0.1	35±13	204
$Ni^{2+}+A^- \rightleftarrows NiA^+$	0—45	0.1	31±6	204
$Ni^{2+}+Gl^-$ [c] $\rightleftarrows NiGl^+$	0—45	—	28±2	205
$NiGl^+ + Gl^- \rightleftarrows NiGl_2$	0—45	—	28±25	205
$Co^{2+}+Gl^- \rightleftarrows CoGl^+$	0—45	—	22±14	205
$CoGl^+ + Gl^- \rightleftarrows CoGl_2$	0—45	—	24±20	205
$Mn^{2+}+Gl^- \rightleftarrows MnGl^+$	0—45	—	16±10	205
$Ni^{2+}+Mal^{2-}$ [d] $\rightleftarrows NiMal$	0—45	—	46±20	206
$Co^{2+}+Mal^{2-} \rightleftarrows CoMal$	0—45	—	68±25	206
$Mn^{2+}+Mal^{2-} \rightleftarrows MnMal$	0—45	—	92±30	206
$Fe^{3+}+Cl^- \rightleftarrows FeCl^{2+}$	10	0	61±4	207
ditto	10	9.72 ($HClO_4$)	23±4	207
»	25	0	58±1	207
»	25	9.72 ($HClO_4$)	24±4	207
»	55	0	53±4	207
»	55	9.72 ($HClO_4$)	20±4	207
$Bi^{3+}+Cl^- \rightleftarrows BiCl^{2+}$	0	4 *M* $HClO_4$	36	208
ditto	10	4 *M* $HClO_4$	36	208
»	40	4 *M* $HClO_4$	32	208
$Bi^{3+}+Br^- \rightleftarrows BiBr^{2+}$	40	4 *M* $HClO_4$	32	208
$Zn^{2+}+4Cl^- \rightleftarrows ZnCl_4^{2-}$	25	2 *m* [$Zn(ClO_4)_2$—$CaCl_2$—H_2O]	70	209
ditto	25	3 *m* ditto	32	209
$Cd^{2+}+4Cl^- \rightleftarrows CdCl_4^{2-}$	25	2 *m* [$Cd(ClO_4)_2$—$CaCl_2$—H_2O]	60	209
ditto	25	3 *m* ditto	57	209

[a] Suc^{2-} = succinate anion; [b] A^- = β-alanite anion; [c] Gl^- = glycinate anion; [d] Mal^{2-} = malonate anion.

The large positive change in heat capacity on complex formation is also indicated by the study of ΔH for the formation of $FeBr^{2+}$ [210] and $CdBr^+$ [211] at different temperatures and by the study of heat capacity in the H_2SO_4—HNO_3—H_2O system [212]. In view of this characteristic

feature of the ΔC_{pk} values, it must be assumed that Spedding and Jones' conclusion that complex formation is responsible for the production of the maximum on the $\Phi Cp = f(m)$ curves for the REE chlorides at high concentrations is incorrect[54,55] (see p. 810).

The positive change in heat capacity on the formation of acido-complexes is attributed to the partial liberation of water from the hydrate sheaths of simple ions and to a reduction of the range over which ions affect the heat capacity of the surrounding water due to a decrease in the overall charge of the particles[209,213-216]. Vasil'ev[207,208,210,217-222] explains this phenomenon on the basis of the view that "icebergs" of water molecules are formed around simple and complex ions, and that these icebergs undergo rearrangement on complex formation.

An interesting feature is that the effect of temperature on ΔC_{pk} in the cases studied[207,208,217] is relatively small (Table 7); at $I = 0$, with increase in temperature from 0° to 50°, the value of ΔC_{pk} decreases by only a few calories. With increase in I the effect of temperature becomes even smaller. This suggests that the decrease in ΔC_{pk} with increase in temperature is due chiefly to the decrease in the heat capacity of the free water. With increase in the ionic strength, the quantity of free water becomes smaller, with a corresponding decrease in the effect of temperature on ΔC_{pk}.[223]

ΔC_{pk} has been determined by the direct calorimetric method for the $Zn(ClO_4)_2-CaCl_2-H_2O$ and $Cd(ClO_4)_2-CaCl_2-H_2O$ systems[209,214-216,226] for several values of the total electrolyte concentration and for different ratios of the quantities of complex-forming species and ligand. The values obtained are the overall values for a mixture of several species of complex, but at high ratios m_{Cl}/m_M they correspond almost completely to the formation of the complexes $ZnCl_4^{2-}aq$ and $CdCl_4^{2-}aq$. After analysing the dependence of ΔC_{pk} on m_{total}, on m_{Cl}/m_M, and on $[Cl^-]_{free}$, the authors cited concluded that the greatest increase in ΔC_{pk} corresponds to the formation of the neutral species, and that ΔC_{pk} is sensitive to the state of the species in the outer sphere.

4. Change in Heat Capacity on the Formation of Ternary and Multi-component Solutions

In addition to the paper already cited[3-6,9-12,15,16,22,23], work in this field has been published by Karapet'yants, Vasilev, and coworkers[91-94,229-237], Latysheva and Andreeva[209,214-216,223,226], and Anderson and coworkers[238,239].

The paper by Karapet'yants, Vasilev, and coworkers are devoted to the study and interpretation of those deviations from additivity which accompany the formation of ternary solutions from two binary solutions when these are isomolal (sometimes isopiestic). Most of the systems studied (mixtures of solutions of alkali and alkaline earth metal halides) do not contain acido-complexes, and the changes in heat capacity accompanying their formation from the binary solutions are extremely small. The authors cited attributed them to slight changes in the structure of the solution and to the redistribution of water between the ions. Work by Anderson and coworkers[238,239] has been carried out in approximately the same direction.

Latysheva and Andreeva[209,214-216,226] studied ΔC_p for the formation of the ternary non-complex-forming solutions $Ca(ClO_4)_2-Zn(ClO_4)_2-H_2O$, $Ca(ClO_4)_2-Cd(ClO_4)_2-H_2O$, and $CaCl_2-Ca(ClO_4)_2-H_2O$ from the corresponding (isomolal) binary solutions. The values obtained are small compared with ΔC_p for the formation of ternary complex-forming systems. The values of ΔC_p are slightly greater in the system formed by solutions of zinc and calcium perchlorates than in the other two systems; in the opinion of the authors cited, this indicates an appreciable redistribution of water between Zn^{2+} and Ca^{2+} cations, which differ significantly in their ability to undergo hydration. Nevertheless, it follows from these papers, and also from the others listed above, that the changes in heat capacity associated only with the redistribution of water between the dissolved electrolytes or with the structural changes in the system on the formation of the ternary solution from the binary solutions are generally small compared with the changes in heat capacity on the dissolution or ionisation of electrolytes, or the formation of acido-complexes. This is evidently related to the fact that the effect of the ions on the heat capacity of the more distant layers of water molecules is much less than that for the nearest molecules.

5. Sharp Change in Heat Capacity within Narrow Ranges of Temperature and Concentration

The few papers which have been published in this field[65,240-245] indicate the possibility of fairly sharp changes in the heat capacity of certain solutions within a narrow range of temperature or concentration. Smirnova and coworkers[240] observed the existence of a maximum on the $\Phi Cp = f(\sqrt{m})$ curve in the range of high concentrations (80–82%) of polyphosphoric acids, and attributed it to a change in the structural form. Latysheva and coworkers[241,242] studied the influence of heating through several degrees on the heat capacity of solutions of strontium perchlorate and manganese sulphate, saturated at temperatures close to the temperature of the change in the composition of the solid phase. The transformations studied were $Sr(ClO_4)_2.4H_2O \rightarrow Sr(ClO_4)_2.2H_2O + 2H_2O$ ($t° = 25.5°$) in the case of strontium perchlorate, and $MnSO_4.5H_2O \rightleftharpoons MnSO_4.4H_2O + H_2O$ ($t° = 27°$) in the case of manganese sulphate. Both systems showed sharp changes in heat capacity, but the form of the curve and the displacement of the temperature of the sudden change with change in concentration are specific for each system. Typical examples of curves for the two systems are shown in Fig. 7. With increase in concentration, the temperature of the sudden change increased in the $Sr(ClO_4)_2-H_2O$ system, and decreased in the $MnSO_4-H_2O$ system. The heat capacity isotherms for these systems also show sharp changes in heat capacity (within a narrow range of concentrations). The phenomena are attributed to a change in the structure of the solutions due to the partial dehydration of the cations, accompanied in the case of the $MnSO_4-H_2O$ system by the formation of acido-complexes. Labowitz and Westrum[243], in a study of the heat capacity of solutions of NH_4F in water at concentrations of 0.005 to 0.50 m and temperatures in the range 55–325°K, found that the heat capacity of the solutions varies very smoothly with temperature at some concentrations, whereas at other concentrations a heat capacity surge is observed at the eutectic temperature. The change from the first solutions to the second apparently corresponds to a significant rearrangement of the solutions within a finite range of concentrations.

In the cases examined, the heat capacity surges were observed at fairly high electrolyte concentrations, so that

they must have been due to changes in the structure of the solution as a whole. At the same time the possibility of a sharp rearrangement in only one component is not excluded. For example, in pure water, breakdown of the collective structure was observed close to 34°.[244] This effect increases when non-polar substances of the benzene type are dissolved in water: the curve giving the temperature dependence of ΔC_p for the dissolution of benzene shows a distinct maximum in the region of 30° (Fig. 8).[245]

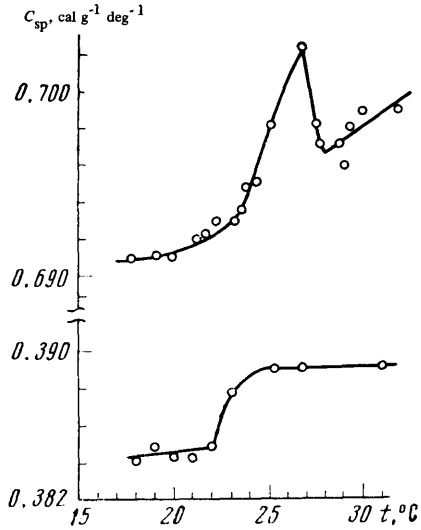


Figure 7. Examples of the form of the temperature dependence of the heat capacity of solutions of $Sr(ClO_4)_2$ (1) and $MnSO_4$ (2) under conditions close to those corresponding to the change in the composition of the solid phase in equilibrium with the solution.

In solutions of strong electrolytes this effect disappears, since the dissolution itself in this case leads to breakdown of the collective structure of water[244]. On the dissolution of substances with a strong ordering influence, on the other hand, the extremal values on the curves giving the temperature dependence of the heat capacity may become even sharper.

Solutions of polyribouridylic, polyriboadenylic, and deoxyribonucleic acids showed sharp heat capacity λ-surges at two temperatures[246]. The cause in this case is apparently the change in the collective hydrophobic interaction of the protein molecules. According to some estimates[247], the hydrophobic interaction between two protein side chains in solution at 25° is characterised by values of ΔC_p in the range from −10 cal mole^{-1} deg^{-1} to −50 cal mole^{-1} deg^{-1}. Berendsen even suggests that hydrophobic bonds are a more important factor in the stabilisation of the native conformation of a protein than intermolecular hydrogen bonds[247]. Breakdown of the hydrophobic interaction is associated with a sharp change in the structure of the surrounding water.

The marked contribution of changes in structure to the value of the heat capacity of solutions may be related to the heat capacity of activation, and moreover it must obviously have a decisive influence on the difference between the isobaric and isochoric heat capacities.

6. Heat Capacity of Activation

This problem was studied by Cobble[248-250], who showed that for the successful development of the theory of reaction rates in aqueous solution there is an extreme lack of data on the relationship between the nature and structure of the activated complexes on the one hand and the values of the energy $\Delta E^{\neq}$, enthalpy $\Delta H^{\neq}$, and entropy $\Delta S^{\neq}$ of activation on the other.

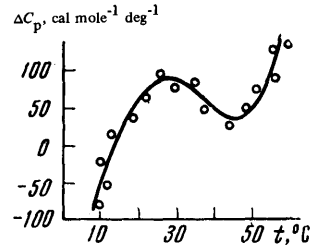


Figure 8. Temperature dependence of ΔC_p for the dissolution of benzene in water.

Cobble assumes that this gap can be filled by studying the heat capacity of activation $\Delta C_p^{\neq}$, which can be determined experimentally (as the temperature coefficient of $\Delta H^{\neq}$) or calculated for an activated complex with a given structural model using the principles of statistical thermodynamics. Additional verification of the description of the symmetry and internal motion in the activated complex is possible by means of a statistical calculation of the $\Delta S^{\neq}$ values, which are related to $\Delta C_p^{\neq}$ by the familiar equation

$$\left(\frac{\partial \Delta S^{\neq}}{\partial T}\right)_p = \frac{\Delta C_p^{\neq}}{T}. \qquad (12)$$

On the other hand, in Cobble's opinion, $\Delta C_p^{\neq}$ can be extimated from experimental data on $\Delta S^{\neq}$ by means of the correspondence principle (p. 808). The results of this estimate for a number of reactions are given in Table 8.

Table 8. Estimated values of $\Delta C_p^{\neq}$ for various reactions[249] at 25°.

Rate-determining reaction	$\Delta C_p^{\neq}]_{25}^{100}$, cal mole^{-1} deg^{-1}
$OCl^- + OCl^- \rightarrow [OClOCl]^{2-\neq}$	98
$[S\dot{O}_3]^{2-} + [S_2O_3]^{2-} \rightarrow [O_3S\dot{O}_2S_2]^{4-\neq}$	75
$[Fe^{\cdot}(CN)_6]^{4-} + [Fe(CN)_6]^{3-} \rightarrow [Fe^{\cdot}(CN)_6 Fe(CN)_6]^{7-\neq}$	52
$HO_2^- + Co^{3+} \rightarrow [HOCo]^{2+\neq}$	$\leqslant 0$
$[Pu^{\cdot}(OH)]^{3+} + Pu^{3+} \rightarrow [Pu^{\cdot}(OH)Pu]^{6+\neq}$	−29
$[Fe^{\cdot}(OH)]^{2+} + Fe^{2+} \rightarrow [F\ddot{e}(OH)Fe]^{4+\neq}$	−35
$Cr^{2+} + [(H_2O)Co(NH_3)_5]^{3+} \rightarrow [Cr(H_2O)Co(NH_3)_5]^{5+\neq}$	~ −40
$H^+ + VO_2^+ + Fe^{2+} \rightarrow [HVO_2Fe]^{4+\neq}$	−53

Unlike reactions in gases, reactions in aqueous solutions may have very large $\Delta C_p^{\neq}$ values, which may be

either positive or negative. In the last case it is possible in principle that above a certain inversion temperature the activation energy will be not positive but negative, since

$$\Delta H^{\neq}_{(T_1)} = \Delta H^{\neq}_{(T_1)} + \Delta C^{\neq}_p (T_2 - T_1) \qquad (13)$$

and the kinetics will become retrograde. The problem of retrograde kinetics is now being studied in Cobble's laboratory.

In the opinion of Arnett and coworkers [251], the fluctuations and irregularity in the experimentally determined values of $\overline{C}^0_{p_2}$ for some substances may be due to fluctuations in the values of $\Delta C^{\neq}_p$.

V. HEAT CAPACITY AT CONSTANT VOLUME C_V

Kozhevnikova and Latysheva [50,171,252] determined C_V and $C_p - C_V$ for aqueous solutions of Mn^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+} perchlorates. Contrary to the previously held opinion, the difference $C_p - C_V$ was found to be fairly large. In addition, the form of the dependence of $\Phi C_p - \Phi C_V$ on the concentration, previously unknown for electrolytes, was determined. All the perchlorates are characterised by a maximum on the $\Phi C_p - \Phi C_V = f(m)$ curve (Fig. 9). To explain the results obtained, these authors put forward a model of the structure of these solutions at different concentrations.

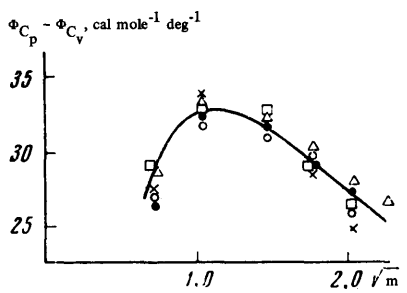


Figure 9. Dependence of the difference $\Phi C_p - \Phi C_V$ for the perchlorates of doubly-charged 3*d* metals (Mn, Co, Ni, Cu, and Zn) on the concentration of the solution.

The determination of C_V has been carried out by Gucker [105,253], but the numerical data [253] are unfortunately not yet available to Soviet readers.

C_V values for solutions of several electrolytes at 25° and 230° have been determined under the direction of Galinker [254,255]. An interesting observation is the marked increase in the difference $C_p - C_V$ with increase in temperature. At the same time there is a sharp decrease in the difference between water and electrolyte solutions. The magnitude of $C_p - C_V$ decreases with increase in concentration at high temperatures, in contrast to the behaviour at low temperatures. The authors cited assume that $C_p - C_V$ is related to the sharp increase in the entropy of the liquid at constant pressure, that is "it is found that a small decrease in the volume of the liquid brings about a marked decrease in the freedom of the thermal motion of the molecules".

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The material reviewed demonstrates the deep and complex relationship between the heat capacity of aqueous solutions of electrolytes and the chemical character of the dissolved ions and the solvent. Without establishing the essential features of this relationship we cannot hope to develop the theory of the problem and solve the corresponding applied problems. At the same time the most rigorous route—from the quantum-mechanical description of the ion–molecule interactions to the macro-properties of solutions via statistical thermodynamics—is as yet too difficult. A method which is more accessible at the present time and therefore more promising (the establishment of the relationship between the chemistry of the micro-reactions in solutions and their properties) involves the search for and the thorough analysis of the regular features of the change in properties from one solution to another on the basis of the periodic classification of the elements. It is the (temporary) impossibility of predicting theoretically all the contributions to the heat capacity of a solution with a given composition which makes necessary an analysis of the regular features for a number of systems related to one another by the periodic classification, since in an analysis of this kind the probability that one of the constituent macro-properties will be missed is decreased sharply [129]. For example, the important contribution of the destructive influence of ions to the heat capacity was detected only in analysis of the regular features of the change in the values of $\overline{C}^0_p$ for series of ions of the alkali and alkaline earth metals and the halogens [36,37,50,171], and not from the heat capacity of solutions of any single electrolyte. The addition of the series of 3*d* metal ions [50–53,81,129,171,175,252,256,257] to these series revealed the effect of the interaction energy of the ions with water on heat capacity, and the study of REE ions revealed the influence of the coordination number of the cations [54,55]. A comparative study of the heat capacity of solutions of the chlorides and perchlorates of the elements of the second main group and side group provided further information on the relationship between heat capacity and the formation of acido-complexes in solution [209,213–216,226].

Thus in order to develop the theory of the heat capacity of solutions, the studies must not be restricted to solutions of the simplest salts, that is the alkali halides, and it is necessary to extend the range of materials studied even further, using the logic of the periodic classification. The fruitful results to be obtained from the use of the periodic classification for practical purposes by the method of comparative calculation have been proved convincingly in a large number of papers [124,154,231,232,258,259]. The method makes it possible in many cases to predict the properties of solutions of compounds which are difficult to obtain.

Nevertheless, the problem of increasing the accuracy of experimental methods for the determination of heat capacity, particularly in dilute solutions, remains urgent. The lack of accurate heat capacity data is at present holding back its theoretical analysis. In view of the exceptional complexity of the interpretation of the heat capacity of solutions, it would be extremely useful to have the results of investigations combining a study of heat capacity with an examination of other properties over a wide range of temperatures and pressures [254,255,260].

The development of new methods for estimating individual contributions to the heat capacity of solutions from the results of spectroscopic measurements of different kinds would be extremely useful. Spectra characterising the weak intermolecular interactions and rotations of molecules would be highly important, since the change in intramolecular vibrations as a result of interactions in aqueous solutions of electrolytes makes only a relatively small contribution to the heat capacity [181]. We can also apparently expect to obtain interesting information from studies of the changes in heat capacity in non-equilibrium processes, for example the so-called heat capacity of transfer C^*, determined in the study of the Soret effect [261-264]. In the opinion of Kennerley and coworkers [262], the effect of transfer makes it possible to obtain a pecture of the state of water which is external with respect to the moving particle, that is the hydrated molecule or ion, whereas an overall property of the solution includes the characteristics of all the particles simultaneously.

One of the most important problems related to the study of the heat capacity of aqueous solutions of electrolytes undoubtedly remains the problem of the development of the theory of the liquid state of water.

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Leningrad State University,
Department of Inorganic
Chemistry

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Double Molybdates and Tungstates of the Rare Earth and Alkali Metals

A.A.Maier, M.V.Provotorov, and V.A.Balashov

Data on the preparation, structure, and various properties of the double tungstates and molybdates (EO_4) of the alkali (M) and rare earth (R) metals with the composition $RM(EO_4)_2$ have been summarised and systematised. The regular features of the change in the symmetry, polymorphism, and nature of the fusion with change in the nature of the alkali and reare earth metals have been examined. The bibliography contains 82 references.

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I. INTRODUCTION

Double molybdates and tungstates of the type $R^{3+}M^{+}(EO_4)_2$, where R represents a rare earth element (REE) or any other tervalent element, M represents an alkali metal, and E represents molybdenum or tungsten, are of considerable interest in connection with their possible use as laser matrices. Up to the present, lasing has been achieved in single crystals of $LaNa(WO_4)_2$,[1] $LaNa(MoO_4)_2$,[2-8] $PrNa(MoO_4)_2$, $TbNa(MoO_4)_2$,[8] $GdNa(MoO_4)_2$,[7] $GdLi(MoO_4)_2$,[9] and $YK(MoO_4)_2$,[10,11] containing Nd^{3+}. The transparency of these crystals over a wide range of wavelengths of the spectrum (0.4–5.0 μ), the high thermal conductivity [22 mW cm^{-1} deg^{-1} for $LaNa(MoO_4)_2$], low lasing threshold [5.5 J for $LaNa(MoO_4)_2$–Nd^{3+}], and the possibility, in principle, of obtaining single crystals with any concentration of active ion, have been noted.

The crystals of many double tungstates and molybdates are characterised by structural disorder, involving the random distribution of R^{3+} and M^{+} in the lattice[12]; the disorder is apparently greater, the closer the radii of these two ions[13,14]; it is revealed in the indistinct nature of the birefringence pattern and in the broadening of the bands in the vibrational absorption, luminescence, and paramagnetic resonance (PMR) spectra[2,3,7,12,15,16]. Two important possible applications of these disordered crystalline systems have been noted: the production of extremely short ($<10^{-11}$ s) giant pulses of coherent radiation in optical quantum generators (OQG) with phasing of the modes; and high-temperature lasing[17].

Almost all double molybdates and tungstates $RM(EO_4)_2$ have now been prepared, their structures and polymorphism have been studied, and their melting points and other physicochemical properties have been determined. Most of these compounds have been obtained in the form of small single crystals suitable for the study of their structures and optical, magnetic, and various other properties. Large single crystals for lasers have been grown for only a few of these compounds, however. The lack of a well-developed technology for the growth of large crystals is retarding the further study of this interesting class of laser material.

The wide variety of properties shown by this group of compounds on the one hand provides the possibility, in principle, of an extensive selection of methods for the preparation of active solids with desirable properties, and on the other hand complicates this selection. In this connection, we have attempted to analyse and systematise the available (in many instances contradictory) data.

As compounds derived from scheelite (by replacing two calcium atoms by R and M atoms), the double compounds $RM(EO_4)_2$ can be classified naturally according to the extent to which the dimensions of the ions R^{3+} and M^{+} differ from those of the calcium ion. This replacement, in addition to the scheelite-like structure, produces a whole set of new structural types. Thus the properties of the double compounds must be related not only to the disordered character of the structure, but also to the actual structures and structural types.

According to Goldschmidt's rule[18], the crystal structure of a compound depends chiefly on the polarisation properties, geometric parameters, and relative numbers of the ions present. The polarisation properties (the nature of the hybridisation) of the ion in complex compounds (to which class the double molybdates and tungstates belong) are suppressed by the large total energy of the lattice[19]. It may therefore be assumed that the structure of $R^{3+}M^{+}(EO_4)_2$ is determined chiefly by the ratio of the dimensions of the ions, which in turn may change with change in temperature, so that it also determines the polymorphism. In the series of normal double molybdates and tungstates $R^{3+}M^{+}(EO_4)_2$, the variable species are R^{3+} and M^{+}, so that the structure and also the degree of disorder will depend on the values of the ionic radii $r_{R^{3+}}$ and $r_{M^{+}}$ (naturally, within the approximation indicated).

Existing systems[20] of ionic radii characterise the values at room temperature, so that it is justifiable to examine the dependence of the symmetry of the structures on $r_{R^{3+}}$ and $r_{M^{+}}$ only for the low-temperature phases. We cannot however reach completely reliable conclusions regarding the crystal system of the low-temperature phase in those cases where some authors have established a polymorphic transition, and others have not detected it, and the problem of whether the crystal systems which they have established correspond to the high-temperature or low-temperature modifications remains open. This ambiguity can be resolved on the basis of the working hypothesis that there is a certain probability of quenching or stabilisation of high-temperature phases at low temperatures either as a consequence of the presence of impurities or as a result of

insufficiently slow cooling in the region of the temperature of the phase transformation.

Comparison of the results obtained by different authors leads to the conclusion that the ability of the high-temperature phases to undergo quenching or stabilisation is a characteristic feature of double tungstates and molybdates, so that the production of a particular modification depends on the method of preparation and subsequent thermal treatment.

II. PREPARATION OF DOUBLE MOLYBDATES AND TUNGSTATES $R^{3+}M^{+}(EO_4)_2$

A bibliography of various methods for the preparation of the double molybdates and tungstates formed by the alkali metals with the REE and Y is given in Tables 1 and 2. The compounds are prepared by precipitation from aqueous solutions (O), by the hydrothermal method (Г), by crystallisation from solutions in melts (P), and by heating mechanical mixtures of the oxides and salts (T). (The preparation of large single crystals by the Czochralski method is denoted by the letter C in the Tables.)

Table 1. Methods for the preparation and the growth of single crystals of double molybdates of the REE (R) and alkali metals (M) $RM(MoO_4)_2$.

R	M				
	Li	Na	K	Rb	Cs
Y	$T^{21,22}$ $P^{23,24}$	$T^{21,22,25}$ $P^{16,23,24,26}$	T^{27} $P^{16,28}$	T^{29}	$T^{30,31}$ $P^{23,31}$
La	$T^{21,32}$ $P^{16,33}$	$O^{34,35,36}P^{16}$ $T^{21,25,37,38}$ $C^{8,37,38,39}$	$T^{21,32}$ $P^{16,21}$	$T^{29,31}$ P^{40}	$T^{21,30,31,32}$ P^{29}
Ce	T^{21} P^{33}	O^{36} T^{21}	T^{21} P^{41}		
Pr	T^{21} P^{33}	$O^{35}T^{21,25}$ $P^{42}C^{8}$	$T^{21,27}$ T^{41}	$T^{21,29,31,43}$ P^{44}	$T^{30,31}$ P^{31}
Nd	$T^{21,45}$ P^{33}	$O^{35}T^{21,25,46}$ $P^{42,47},C^{8}$	$T^{21,27,48}$ P^{41}	$T^{21,29,31,44}$	$T^{30,31}$
Sm	$T^{21,45}$ P^{39}	$T^{21,25}$ $P^{42,47}$	$T^{21,48}$ P^{41}	$T^{21,29,31,43}$	$T^{30,31}$
Eu	T^{21} $P^{23,24,33}$	$T^{21,25}$ $P^{23,42,47}$	$T^{21,48}$ $P^{22,41}$	$T^{21,29,31,43}$ P^{23}	$T^{30,31}$ $P^{23,49}$
Gd	$T^{21,45}$ P^{33}	$O^{50}T^{21,25}$ $P^{42,47}$	$T^{48,51}$ P^{41}	$T^{21,29,31,49}$	$T^{30,21}$
Tb	$T^{21,52}$ $P^{22,24,33}$	$T^{21,52}$ $P^{23,42,47}C^{8}$	$T^{21,48,52}$ $P^{23,41}$	$T^{21,43}$ P^{23}	$T^{30,31}$
Dy	$T^{21,45,53}$ $P^{33,54}$	$T^{21,25,55}$ $T^{42,47}$	$T^{21,48,51}$ P^{41}	$T^{21,29,41,43}$	$T^{30,31}$
Ho	$T^{21,53}$ P^{33}	$O^{50}T^{21,25,55}$ $P^{42,47}$	$T^{21,48,51}$	$T^{21,29,41,43}$	$T^{30,31}$
Er	$T^{21,53}$ P^{33}	$O^{56}T^{21,24,55}$ $P^{42,47}$	$T^{21,27,48,51}$ P^{41}	$T^{21,29,41,43}$	$T^{30,31}$ O^{56}
Tm	$T^{21,52}$ P^{33}	$T^{21,25,52}$ $P^{42,7}$	$T^{21,48,52}$ P^{41}	$T^{21,29,41,43}$	$T^{30,31}$
Yb	$T^{21,52}$ P^{33}	$T^{21,25,52}$ $P^{42,47}$	$T^{19,25,83}$ $P^{21,48,52}$	$T^{21,29,41,43}$	$T^{21,30,31}$
Lu	$T^{21,45,52}$ P^{33}	$T^{21,52}$ P^{42}	$T^{21,48,52}$ P^{41}	$T^{21,29,41,43}$	$T^{21,30,31}$

1. Precipitation from Aqueous Solutions

The double compounds $RM(EO_4)_2$ are precipitated by mixing aqueous solutions of M_2EO_4 and a salt of the tervalent element. Both the direct (addition of M_2EO_4 solution to a solution of the REE salt) and the reverse order of mixing are used. The second alternative appears less reliable, as a consequence of the hydrolysis of the salt of the tervalent element when it is added to the MEO_4 solution, which has an alkaline reaction [61].

It has not been possible to obtain the sodium double tungstates with the REE from La to Sm, or any of the lithium double tungstates, by simply mixing the solutions [61]. $RNa(WO_4)_2$ (R = La, Ce, Pr, or Nd) have been obtained only in neutral medium; for this purpose, nitric acid was added to Na_2WO_4 solution to pH 8, so that on mixing with $R(NO_3)_3$ solution the mother-liquor had pH 7. [35] The corresponding double molybdates are formed by simply mixing the solutions.

Table 2. Methods for the preparation and the growth of single crystals of double tungstates of the REE (R) and alkali metals (M) $RM(WO_4)_2$.

R	M				
	Li	Na	K	Rb	Cs
Y	T^{57} $P^{23,58}$	$O^{61}T^{25,59,60}$ $P^{12,23,62,63}$ C^{63}	$O^{61}T^{61,64}$ P^{65}	$O^{61}T^{54,61}$ P^{23}	$O^{61}T^{54,61}$ P^{23}
La	P^{58}	$O^{35}T^{25,59,60}$ $P^{63,66}C^{39,62,63}$	$O^{61}T^{15,61}$ $P^{23,65,66}$ $Г^{66}$	$O^{61}T^{54,61}$	$O^{61}T^{54,61}$
Ce	T^{68-70} $Г^{68,69}P^{23}$	$O^{35}Г^{68}$ P^{66}	$T^{15}Г^{67,68}$ $P^{65,66}$		
Pr	T^{68-70} $Г^{68,69}P^{58}$	$O^{35}T^{25,59}$ $Г^{68}C^{72}$	$T^{15}Г^{67,68}$ P^{65}	T^{54}	T^{54}
Nd	$T^{68,69}$ $Г^{68,69}P^{58}$	$O^{35}T^{25,59,60}$ $Г^{69,71}P^{73}$	$O^{61}T^{15}$ $Г^{67,68,71}$ $P^{61,65}$	$O^{61}T^{54,61}$	$O^{61}T^{54,61}$
Sm	P^{58}	$O^{61}T^{25,59,60}$ P^{62}	$O^{61}T^{15,61}$ P^{65}	$O^{61}T^{54,61}$	$O^{61}T^{54,61}$
Eu	$P^{23,58}$	$O^{61}T^{25,60}$ $P^{23,62}$	$O^{61}T^{15,61}$ $P^{23,65}$	$O^{61}T^{54,61}$ $P^{23,75}$	$O^{61}T^{54,61}$ $P^{23,75}$
Gd	P^{58}	$O^{61}T^{25,59,60}$ $P^{23,62,72}$ $C^{7,72}$	$O^{61}T^{15,61}$ P^{65}	$O^{61}T^{54,61}$	$O^{61}T^{54,61}$
Tb	$P^{23,58}$	$O^{61}P^{23,62}$	$O^{61}T^{15,61}$ P^{65}	$O^{61}T^{54,61}$ P^{23}	$O^{61}T^{54,61}$
Dy	P^{58}	$O^{61}T^{25,60}$ P^{62}	$O^{61}T^{15,61}$ P^{65}	$O^{61}T^{54,61}$ P^{76}	$O^{61}T^{54,61}$ P^{23}
Ho	P^{58}	$O^{61}T^{25,60}$ P^{62}	$O^{61}T^{15,61}$ P^{65}	$O^{61}T^{54,61}$	$O^{61}T^{54,61}$
Er	P^{58}	$O^{61}T^{25,60}$ P^{62}	$O^{61}T^{15,61}$ P^{65}	$O^{61}T^{54,61}$	$O^{61}T^{54,61}$
Tm	P^{58}	$T^{25,60}$ P^{62}	T^{15} P^{65}	T^{54}	T^{54}
Yb	T^{76} $P^{58,76}$	$O^{61}P^{25,60}$ P^{62}	$O^{61}T^{15,61}$ P^{65}	$O^{61}T^{54,61}$ P^{74}	$O^{61}T^{54,61}$ P^{74}
Lu	$T^{58}P^{63}$ C^{63}	$P^{60,62}$	T^{15} P^{65}	T^{54}	T^{54}

In all cases the normal tungstate or molybdate is precipitated first; on standing, this reacts with the excess of M_2EO_4 in the solution to form the double salt [36,61]. The double molybdates with sodium and potassium (unlike those with rubidium and caesium) are readily decomposed by water. Since departures from stoichiometry take place when these precipitates are washed with water, the removal of mother-liquor in a press has been proposed [61]. At low concentrations of the REE salt (≤ 0.01 M), the sodium and potassium double molybdates (unlike the

rubidium and caesium compounds) are not formed[61].

The data given show that the stability of the double tungstates, under the conditions of preparation from solution, increases from Li to Cs. In view of the similarity in the chemical properties of molybdates and tungstates, it may be assumed that the same regular features are observed for the double molybdates

The precipitated double molybdates formed by sodium with the REE from La to Nd contain one molecule of water of crystallisation[34-36]. The removal of water and the crystallisation of anhydrous $NdNa(MoO_4)_2$ begin at 540°.[34]

The compositions of the hydrated tungstates, and the temperatures of their dehydration and crystallisation with the formation of the anhydrous double compounds are given in Table 3.

Table 3. Characteristics of double tungstates $RM(WO_4)_2$ obtained by precipitation from aqueous solutions.

Composition of the air-dry precipitate	Temp. of complete dehydration, °C	Temp. of crystallisation of the anhydrous compound, °C	References
$NdNa(WO_4)_2 \cdot 5H_2O$.	>300	540	35
$RNa(WO_4)_2 \cdot 2.5H_2O$, R=Sm — Er, Yb, Y.	155—190	460—570	61
$RK(WO_4)_2 \cdot 2.5H_2O$, R = La, Nd, Sm.	250—260	540—610	61
$RK(WO_4)_2 \cdot 1.5H_2O$, R = Sm — Er, Yb, Y.	100—150	615—830	61
$RRb(WO_4)_2 \cdot 1.5H_2O$, R = La, Nd.	190—230	560÷730	61
$RRb(WO_4)_2 \cdot 1.5H_2O$, R=Sm — Er, Yb, Y.	120—130		61
R = Er, Tm, Y, Lu	360		29
$LaCs(WO_4)_2 \cdot 1.5H_2O$,	210	550	61
$RCs(WO_4)_2 \cdot H_2O$, R=Nd — Er, Yb, Y.	140—180		61

2. Hydrothermal Preparation of $RM(EO_4)_2$

This method has been used for the preparation of the double compounds $RM(EO_4)_2$ only by Klevtsov and Kharchenko[71] (Table 2). They prepared crystals of $RLi(WO_4)_2$, $RNa(WO_4)_2$, and $RK(WO_4)_2$ (where R = Ce, Pr, or Nd), and also $LaK(WO_4)_2$, by spontaneous nucleation under isothermal conditions in 8—12 cm^3 capacity autoclaves with titanium linings.

For the lithium—REE double tungstates, the best results from the viewpoint of yield (70%) and crystal size (up to 3 mm) were obtained with a charge consisting of a heated mixture of the oxides R_2O_3 and WO_3 with molar ratio 1 : 2, and 20—30% LiCl solution as solvent, at 525—550° with a filling factor of 50—60%.

The compounds $RNa(WO_4)_2$ were obtained under hydrothermal conditions in the form of fine crystals with dimensions up to 0.3 mm. The optimal conditions of crystallisation were the same as those for $RLi(WO_4)_2$.

The potassium double compounds were prepared under hydrothermal conditions at 500—600° in 50% KCl solution. At lower concentrations, non-stoichiometric crystals with variable composition $R_{1-x}K_{1-3x}(WO_4)_2$ are formed.

At the comparatively low temperatures characteristic of the hydrothermal method of preparation, the lithium double molybdates crystallise in the triclinic modification, and the potassium compounds in the monoclinic form. When heated above 800°, these phases undergo monotropic conversion into the tetragonal (scheelite) and monoclinic [analogous to $Nd_2(WO_4)_3$] modifications respectively, which are obtained when other methods of preparation are used (Table 2). The sodium REE tungstates are tetragonal for all methods of preparation. The similarity in the ionic radii of Na^+, R^{3+}, and Ca^{2+} evidently facilitates the preservation of the $CaWO_4$ structure[68].

3. Crystallisation of $RM(EO_4)_2$ from Molten Solutions

This method was used to prepare the first double compounds of the type $R^{3+}M^+(EO_4)_2$ [66] (if we exclude the work of Carobbi[36], who precipitated $LaNa(MoO_4)_2$ from aqueous solutions). Several versions of the method are now employed, and in most cases spontaneous crystallisation is used.

Alkali metal chlorides or tungstates (or molybdates) are used as solvents. The latter are more convenient, since they undergo little volatilisation[63] under the crystallisation conditions, have lower melting points, and do not contaminate the crystals with foreign ions.

The high volatility of chlorides can be used to grow crystals by evaporation of the solvent (chloride) from the corresponding molten salts at a constant temperature (700—750°, 10 h).[29,31,40,54] Most frequently, after being heated for 3—20 h in the superheated (1100—1250°) state, the solution is cooled slowly (2—3 deg h^{-1}) to a temperature below the melting point of the eutectic (~700°). The subsequent cooling is carried out more rapidly (~25 deg h^{-1}).

The charge is introduced into the solvent in all possible forms: the oxide R_2O_3, mixtures of the oxides R_2O_3 + $3EO_3$, R_2EO_4, $RM(EO_4)_2$, etc. The only condition is that the ratio of the components of the molten mixture should ensure the formation of the double compound and the solvent in the optimal proportions.

Sometimes, in order to obtain large crystals of $RM(EO_4)_2$, sufficient EO_3 is added to the solvent M_2EO_4 to form $M_2E_2O_7$, which has a higher "capacity" as solvent, as a consequence of the decrease in the EO_4^{2-} concentration with the formation of $E_2O_7^{2-}$.[26] This also explains the existence, on the ternary diagram of the $Na_2O—Gd_2O_3—Mo_2O_6$ system[77], of optimal composition ranges for the production of relatively large crystals. The solidified $M_2E_2O_7$ solvent, however, can be washed from the crystal only with concentrated MOH solution[26], whereas M_2EO_4 is readily removed with water. Moreover, the crystallisation from highly concentrated solutions takes place at a high rate, a large number of crystallisation centres are produced, and entrainment of the solvent by the rapidly growing faces of the crystals takes place. Transparent crystals without inclusions have been obtained only at a molar ratio $R_2(WO_4)_2 : Na_2WO_4 \leq 1 : 9$ (R = Y, La, Lu), at a rate of growth equal to 0.020—0.025 mm h^{-1}.[63] Reverse rotation (60 r.p.m.) of the crucible, beginning at a temperature 10—15 deg below the temperature of the start of crystallisation, made it possible to reduce by an order of magnitude the quantity of crystals of these compounds forming spontaneously.

Individual attempts to grow single crystals on seed crystals and by pulling (Czochralski method) from the melt solutions have been made. $EuCs(MoO_4)_2$ [49] and $RNa(WO_4)_2$, where R = Y, La, and Lu,[63] have been prepared in this way. In the last cases, growth took place in the upper part of a cylindrical quartz vessel containing the melt under conditions of a temperature gradient or a temperature drop (with the use of a diaphragm).

4. Preparation by Heating a Mechanical Mixture

The phase composition of the original mixture can represent any stoichiometric combination of thermally unstable salts of the rare earth and alkali metals and the products of their reaction with one another. It determines the chemistry of the process and hence the minimal temperature of heating.

It has been suggested [25,46] that the preparation of $RNa(EO_4)_2$, where R = La or Nd, by the action of heat on $R_2O_3 + 4EO_3 + Na_2CO_3$ and $R_2O_3 + EO_3 + Na_2EO_4$ mixtures involves the formation of amorphous sodium molybdates and tungstates $Na_2E_4O_{13}$ with their subsequent active reaction with R_2O_3, and that the preparation by the action of heat on an $Nd_2(MoO_4)_3 + Na_2MoO_4$ mixture involves the formation of the intermediate compound $NdNa_5(MoO_4)_4$. The formation of the molybdate $NdNa(MoO_4)_2$ is complete at 500° in the first case and at 600° in the second case. It has also been noted that the formation of the double tungstates takes place at higher temperatures (~750° for the ternary mixture). Other authors (see bibliography in Tables 1 and 2) prepared double molybdates and tungstates by heating at 500–900° and 600–1100° respectively for periods of 8–100 h. The possibility of carrying out the preparation over a wide range of temperatures makes it possible in some cases to obtain various polymorphic modifications immediately [21,43,57].

III. POLYMORPHISM

Comparison of the results obtained by different authors in the thermographic study of polymorphism with the methods of preparation of the compounds which they studied reveals a curious feature. In some cases, transformations which could not be detected in the study of compounds obtained from solutions in a melt have been clearly revealed when the same compounds were prepared by the sintering of solid mixtures.

For sodium and lithium double molybdates it has been possible to establish the existence of transitions (Tables 4 and 5) only after they had been prepared by heating mechanical mixtures with subsequent fusion and slow cooling of the melt. Crystals of the same compounds grown from molten solutions do not show any effects. It may therefore be assumed that in the first case a low-temperature form is obtained, and in the second case a high-temperature form. Both were found to be tetragonal (scheelite type). The weak reversible effects observed on the DTA curves when these compounds are heated indicate only slight rearrangement of the structure [52].

Table 4. Structures and polymorphism of double molybdates of the REE (R) and alkali metals (M) $RM(MoO_4)_2$ (1).

	M	Li	Na	K	Rb	Cs
R	r (2)	0.68	0.98	1.33	1.49	1.65
Y	0.97	T [21,33] 0.82 0.29	T [21,23,25] 0.98 0.01	550 [28,51] (3) T [28] 1.15 0.36	P [29] 1.23 0.60	M [31] 1.31 0.68
La	1.04	T [21,33] 0.86 0.36	T [21,25,34,35,38] 1.01 0.06	T [21,41] (4) 1.18 0.29	T [21,29,40,43] 740 [31] (5.6) M [74]500 [74] M [29,43,51] 1.26 0.45	T [30,31] (4) 950 [31] (7) 1.34 0.61
Ce	1.02	T [21,33] 0.85 0.34	T [21,35] 1.00 0.04	T [21,41] (4) 1.18 0.31	1.26 0.47	(7) 1.34 0.63
Pr	1.00	T [21,33] 0.84 0.32	T [21,25,35,42] 0.99 0.02	T [21,41] (4) 810 [41] 685 [27] 1.16 0.33	T [29] 680 [21,31,43,44] (8) P[74]450 [44] 500 [31] P [29,44] 1.24 0.49	M [31] 1.32 0.65
Nd	0.99	T [21,33] 0.84 0.31	T [21,25,35,42] 0.98 0.01	T [21,41] (9) 780 [27] 680 [27] M [48] 1.16 0.34	T [21,29] 730 [31,43] P [74]510 [31] P [29] (10) 1.23 0.50	M [31] 1.32 0.66
Sm	0.97	T [21,33] 0.82 0.29	T [21,25,42] 0.98 0.01	M [21,48] 1.15 0.36	T [29]860 [31] P [74]510 [31] P [29] (10) 1.23 0.52	M [31]505 [31] M [31] 1.31 0.68
Eu	0.97	T [21,33] 0.82 0.29	T [21,25,42] 0.98 0.01	M [48] M [21]Tp [48] 1.15 0.36	T [29]920 [31] P [74]505 [31] P [29] 1.23 0.52	M [31] 500 [31] M [31] 1.31 0.68
Gd	0.94	T [21,33] 0.81 0.26	T [21,25,42] 0.96 0.94	885 [51] 545 [51] Tp [48] 1.14 0.39	T [74] P [74]520 [31] P [29] (10) 1.22 0.55	M [31] 505 [31] M[31] 1.30 0.71
Tb	0.89	T [21,23,33] 490 [52] T(11) 450 [52] T [52] 0.78 0.21	T [21,42] T [52] 0.94 0.09	P [41,52] (12) 540 [52] (13) Tp [48] 1.11 0.44	T (15) P (12) 520 (14) P (10) 1.19 0.60	M (14) 500 (14) M (14) 1.27 0.76
Dy	0.88	T [21,33,54] 530 [55] T [53] 0.78 0.20	T [21,25,47] T (11) 0.93 0.10	P (12) 530 [51] (13) P [41,48,52] 1.10 0.45	T (15) P [74] 520 [31] P [29] (10) 1.18 0.61	M (14) 500 (14) M [31] 1.26 0.77
Ho	0.86	T [21,33] 520 [53] T [53] 0.77 0.18	T [21,25,47] T (11) 0.92 0.12	P (12) 545 [51] (13) P [41,48,51] 1.10 0.47	T (15) P [74] 520[31] P [29] (10) 1.18 0.63	Γ [31] 980 [31] M [31] 500 [31] M [31] 1.26 0.79

(continued).

Table 4 (continued).

	M	Li		Na		K		Rb		Cs	
R	r (2)	0.68		0.98		1.33		1.49		1.65	
Er	0.85	T [21,33] 515 [53] T [53]	0.76 0.17	T [21,25,47] T (11)	0.92 0.13	Γ [21] P (12) 550 [51] (13) P [41,48,51]	1.09 0.48	Γ [29] 910 [31] P [74] 530 [31] (16) P [21] (10)	1.17 0.64	Γ [31] 905 [31] M [31] 520 [31] M [31]	1.25 0.80
Tm	0.85	T [21,33] 515 [52] T (11) 450 [52] T [52]	0.76 0.17	T [21,25,47] 580 [52] T [52]	0.92 0.13	Γ [21] P (12) 640 [41] (17) P (18) 515 [41,52] P [41,48,52]	1.09 0.48	Γ [29] 850 [31] M [74] 530 [31] M [29] (19)	1.17 0.64	Γ [31] 820 [31] M [31] 510 [31] M [31]	1.25 0.80
Yb	0.81	T [21,33] 510 [52] T (11) 419 [52] T [52]	0.74 0.13	T [21,25,47] 575 [52] T (11) 505 [52] T [52]	0.90 0.17	Γ [21] 875 [41,52] P [41,48,52]	1.07 0.52	Γ [21,29,43] 750 [31,43] M [74] 530 [31] M [29] (19)	1.15 0.68	Γ [21,30,31] 750 [31] M [31] 530 [31] M [31]	1.23 0.84
Lu	0.80	T [21,33] 500 [52] T (11) 450 [52] T [52]	0.74 0.12	T [21,47] 575 [19] T [52]	0.89 0.18	Γ [21] 825 [41,52] P (12) 535 [52] P [41,48]	1.06 0.53	Γ [21,29,43] 720 [31,43] M [74] 540 [31] M [29] (19)	1.14 0.69	Γ [21,30,31] 700 [31] M [31] 520 [31] M [31]	1.22 0.85

*See footnotes to Tables 4 and 5.

Table 5. Structures and polymorphism of double tungstates of the REE (R) and alkali metals (M) $RM(WO_4)_2$ (1).

	M	Li		Na		K		Rb		Cs	
R	r (2)	0.68		0.98		1.33		1.49		1.65	
Y	0.97	T [57,58] 910 [57] (20) M [58] 715 [42] M (14)	0.82 0.29	T [12,25,60,62]	0.98 0.01	1009 [28,64] (21) M [28,79]	1.15 0.36	M [54]	1.23 0.60	Γ [54] M [54]	1.31 0.68
La	1.04	T [58]	0.86 0.36	T [25,35,60,62,80]	1.01 0.06	M [15,23] (22,23)	1.18 0.29	T [54] 815 [54] M [54]	1.26 0.45	T [54] 910 [54]	1.34 0.61
Ge	1.02	T [23,68,69] (24)	0.84 0.32	T [25,62]	1.00 0.04	M [15] (22,23) 740 [15] M (20)	1.18 0.31		1.26 0.41		1.34 0.63
Pr	1.00	T [32,68,69] (24)	0.84 0.32	T [25,35,59]	0.99 0.02	T [54] 950 [54] P [54] 825 [54] M [15,68,71] (22,23) M (23)	1.16 0.33	M [54]	1.24 0.49	M [74] 350 [74] M [74]	1.32 0.65
Nd	0.99	T [32,68,69] 665 [82] T [32,48,68,69] (24)	0.84 0.31	T [25,35,59,60]	0.98 0.01	T [54] 830 [54] M [15,68,71] (22,23) 870 [61] M (23)	1.16 0.34	M [54]	1.24 0.50	M [74] 380 [54] M [74] (25)	1.32 0.66
Sm	0.97	T [48,58]	0.82 0.29	T [25,59,60,62]	0.98 0.01	T [74] 800 [54] M [15] (22,23) 1010 [65] M [15,65] (25)	1.15 0.36	M [54]	1.23 0.52	M [74] 400 [54] M [74] (26)	1.31 0.68
Eu	0.97	T [32,48,75]	0.82 0.29	T [25,60,62]	0.98 0.01	M [74] 800 [54] M [15] (25) 1000 [15] (25) M [15,65,79] (27)	1.15 0.36	M [23,54]	1.23 0.52	M [74] 400 [54] M [74] (26)	1.31 0.68
Gd	0.94	T [48,58]	0.81 0.26	T [25,60,62,80]	0.96 0.04	M [74] 860 [54] M [15] (25) 1005 [65] M [65,79] (27)	1.14 0.39	M [54]	1.22 0.55	M [74] 400 [54] M [74] (26)	1.30 0.71
Tb	0.89	T [48,58] 744 [58] M [48] M [48,58]	0.78 0.21	T [62]	0.94 0.09	M (25) 1080 [65] M [15,65] (27,28)	1.11 0.44	M [74] 800 [55] M [23,54]	1.19 0.60	M [74] 400 [54] M [74] (26)	1.27 0.76
Dy	0.88	T [48,58] 840 [58] M [48,58]	0.78 0.20	T [25,60,62]	0.93 0.10	M (25) 1025 [65] 1040 [61] M [15,65] (27)	1.10 0.45	M [74] 800 [54] M [54]	1.18 0.61	M [74] 400 [54] M [74]	1.26 0.77
Ho	0.86	T [48,58] 882 [58] M [48,58]	0.77 0.18	T [25,60,62]	0.92 0.12	M (25) 1025 [65] 1010 [61] M [15,65] (27)	1.10 0.47	M [74] 800 [54] M [54]	1.18 0.63	Γ [74] 1100 [54] M [74] 400 [54] M [74] (29)	1.26 0.79
Er	0.85	T [48,58] 983 [58] M [48] M [48,58]	0.76 0.17	T [25,60,62]	0.92 0.13	M (25) 1040 [65] 1055 [61] M [15,65] (27)	1.10 0.48	M [74] 830 [54] M [54]	1.17 0.64	Γ [54] 1000 [54] M [74] 400 [54] M [74] (29)	1.25 0.80
Tm	0.85	T [48,58] 976 [58] M [48] M [48,58]	0.76 0.17	T [25,60,62]	0.92 0.13	M (25) 1030 [65] 1060 [61] M [15,65] (27)	1.09 0.48	Γ [54] 1020 [54,74] M [74] 830 [54] M [54]	1.17 0.64	Γ [54] 970 [54] M [74] 440 [54] M [74]	1.25 0.80
Yb	0.81	M [48,58,76,81] (30)	0.74 0.13	T [25,60,62]	0.90 0.17	M (25) 1030 [65] 1060 [61] M [15,65] (27)	1.07 0.52	Γ [54] 920 [54] M [74] 850 [54] M [54]	1.15 0.68	Γ [54] 900 [54] M [74] 400 [54] M [74] (31)	1.23 0.84
Lu	0.80	M [48,58] (30)	0.74 0.12	T [60,62]	0.89 0.18	M (25) 1060 [65] M [15,65] (27)	1.06 0.53	Γ [54] 900 [54] M [74] 870 [54] M [54]	1.14 0.69	Γ [54] 850 [54] M [74] 500 [54] M [74] (31)	1.22 0.85

Footnotes to Tables 4 and 5.

(1) The following symbols are used in Tables 4 and 5: T—tetragonal, P—orthorhombic, M—monoclinic, Tp.—triclinic, Г—hexagonal.
The Tables are divided into blocks, each of which corresponds to a particular double compound. The lower part of each block contains the low-temperature modification, the upper part the high-temperature modification, and the central part the intermediate phase; the temperature (°C) of the phase transformations are given on the right. The values of Δr and r_{av} are given in the lower right-hand corner of the block.
(2) The ionic radii are taken from Ref. 18.
(3) According to Ref. 27, there is no polymorphic transformation.
(4) In our opinion, polymorphism is observed here, and the authors cited obtained the quenched high-temperature forms.
(5) According to Ref. 39, there is no polymorphic transformation.
(6) According to Ref. 43, the temperature of the transformation is 690°.
(7) According to our ideas, the low-temperature phase should have monoclinic or orthorhombic symmetry.
(8) In Ref. 21, a single polymorphic transformation was observed at 700°.
(9) In Ref. 48 it is reported that the high-temperature phase is isostructural with the high-temperature modification of $NdK(WO_4)_2$.
(10) In Refs. 21 and 43 the symmetry was not determined, but it was established that the compound is isostructural with PrRb molybdate, which has orthorhombic symmetry.
(11) We assume tetragonal symmetry here.
(12) Examination of the diagram in Fig. 1 indicates that this is apparently an orthorhombic phase.
(13) According to Ref. 41 there is no polymorphic transformation.
(14) The authors' suggestion.
(15) Quenching of the specimens from temperatures close to the melting points[74] gave a mixture of a tetragonal phase (isostructural with the high-temperature phases of $RRb(MoO_4)_2$ with R = La–Gd) and an orthorhombic phase.
(16) In Ref. 43, a single polymorphic transformation was established at 730° (the measurements were made up to 800°). The low-temperature phase was found to be tetragonal, and the high-temperature phase was found to be isostructural with $PrPb(MoO_4)_2$, orthorhombic[44]. Quenching of $ErRb(MoO_4)_2$ from 650–700° into liquid nitrogen gives a monoclinic modification of the same type as the low-temperature modifications of the rubidium molybdates formed by thulium, ytterbium, and lutetium.
(17) The second polymorphic transformation at 640° in Ref. 52 was not established.
(18) If the orthorhombic structure is stable above 640° [see (12)], then the phase between 515° and 640° is also orthorhombic, since it cannot have a lower symmetry than the low-temperature phase, which has been found to be orthorhombic[41,48,52].
(19) In Refs. 21 and 43, the compound was found to have a tetragonal low-temperature modification, and a low-temperature polymorphic transformation was not detected.
(20) In Ref. 58 the temperature of the phase transformation was found to be 904°.
(21) In Ref. 28 it was suggested that the high-temperature modification has a tetragonal structure.
(22) In Ref. 8 the high-temperature phase was found to have a tetragonal structure with monoclinic distortion.
(23) According to Refs. 65 and 79, polymorphic transformations are not observed.
(24) Hydrothermal preparation[68,69] gave monoclinic crystals.
(25) According to Refs. 43 and 71, the low-temperature form of $RK(WO_4)_2$, where R = La–Nd, has a monoclinic structure. According to Ref. 8, these phases are isostructural with the high-temperature modifications of $RK(WO_4)_2$, where R = Sm–Lu. They are therefore monoclinic, since the symmetry of the high-temperature modification is never lower than that of the low-temperature phase, and the latter, for $RK(WO_4)_2$, where R = Sm–Lu, are monoclinic[15,65,79]. In the case of Lu, the high-temperature modification is apparently hexagonal (see section headed "Fusion").
(26) The low-temperature phase is isostructural with the low-temperature modification of $PrCs(WO_4)_2$.[54]
(27) This phase is isostructural with the low-temperature modification of $YK(WO_4)_2$.[15,65]
(28) In Ref. 76, the structure was found to be triclinic.
(29) The low-temperature phase is isostructural with the low-temperature modification of $YCs(WO_4)_2$.[54]
(30) In Ref. 58 it is suggested that the temperature of the phase transformation is so close to the melting point that the low-temperature monoclinic modification crystallises immediately.
(31) The low-temperature phase is isostructural with the low-temperature modification of $YCs(WO_4)_2$.[54]

It is probable that almost all other $RLi(MoO_4)_2$ and $RNa(MoO_4)_2$ have been obtained in the form of stabilised or quenched high-temperature phases.

The RK molybdates are characterised by a large number of clearly defined polymorphic transitions. The isostructural tetragonal phases $RK(MoO_4)_2$, where R = La–Nd,

prepared from solution in a melt[41] and by sintering mechanical mixtures[21], are probably high-temperature phases, since $NdK(MoO_4)_2$, prepared by the methods of ceramic technology[48], was obtained in two forms: a high-temperature monoclinic distorted scheelite form, corresponding to the tetragonal form[41], and a low-temperature monoclinic form.

$YK(MoO_4)_2$ crystals, obtained from solution in a melt, were found to be orthorhombic[41]. When heated, they underwent a polymorphic transformation[28]. The orthorhombic structure can therefore be regarded as the low-temperature form, although there is still some doubt regarding this conclusion, since the X-ray diffraction pattern for this compound, obtained by sintering mechanical mixtures, contains a large number of lines, the splitting of which indicates a low-symmetry, apparently triclinic, structure[21].

The RK molybdates from Dy to Lu [41,48] and the high-temperature (orthorhombic) modification of $TbK(MoO_4)_2$ [48] are isostructural with the double molybdate $YK(MoO_4)_2$. Crystallisation from solution in a melt[41] gave only this structure of $TbK(MoO_4)_2$, which does not exhibit polymorphism. In this case, therefore, stabilisation of the orthorhombic phase takes place under the conditions of growth. This phenomenon is of undoubted importance for the growth of single crystals.

The crystals obtained from solutions in a melt[41] for the most part undergo high-temperature polymorphic transformations (Table 3). Low-temperature transformations have been detected in the study of the equilibrium diagrams[51] of compounds obtained by sintering mechanical mixtures with subsequent fusion of the sinter and slow cooling[51,52]. The low-temperature transitions in all cases are accompanied by weak thermal effects.

Mokhosoev and coworkers[21] assumed for the potassium molybdates from Er to Lu not the orthorhombic structure, as all other authors have done (Table 4), but a hexagonal structure. At the same time, X-ray diffraction studies[78] of the orthorhombic crystals of $YK(MoO_4)_2$ have shown that their structure is close to hexagonal. From the analogy between the rubidium and caesium double molybdates, we have classified the hexagonal phases as high-temperature phases (Table 3).

Most rubidium and caesium REE molybdates show low-temperature phase transformations (Table 3), which give weak endothermic effects on the thermograms obtained by heating[31], and which do not lead to marked changes in structure.

At high temperatures, the rubidium and caesium double molybdates of the heavy REE become hexagonal (Table 4). In the three-dimensional diagram of phase transformations (Fig. 1), which we constructed from published data, the right-hand upper corner shows the range of existence of the high-temperature hexagonal phase, bounded below by the surface *1*, *2*, *3*, *4*, *5*, *6*, *7*. It can thus be seen that the high-temperature phases of the potassium molybdates of Lu and Yb (and possibly also Tm and Er) should be similar to the high-temperature phases of the caesium and rubidium double molybdates with the heavy REE, that is they should be hexagonal.

A noteworthy feature is that the temperatures of the low-temperature transformations for almost all double molybdates are approximately the same (the surface *14*, *15*, *16*, *17*, *18*, *19*, *20*, *21*, *22*, *23*, *24*, *25*, *26* in Fig. 1). In the diagram, a single overall surface has been drawn through the points corresponding to these transitions (in some regions it is "split" into two surfaces close together). In fact, these transformations have much in common: they are difficult to detect, apparently as a consequence of stabilisation of the high-temperature phase; they give weak thermal effects; and they do not lead to a change in symmetry. Their nature has not yet been established. It is quite possible that this surface has a "gap" in the region of the lithium and sodium double molybdates of the light REE, and their low-temperature transformations are even more difficult to detect.

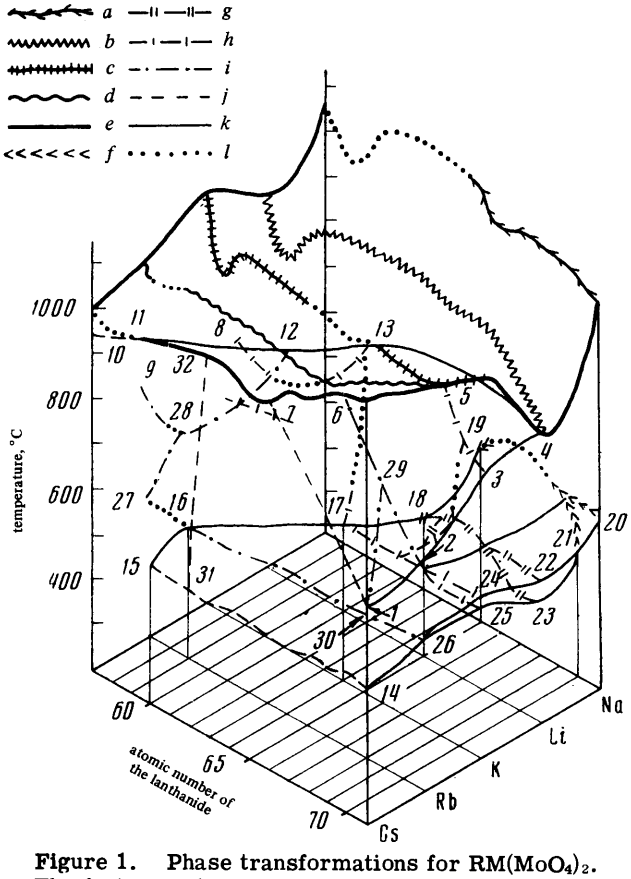


Figure 1. Phase transformations for $RM(MoO_4)_2$. The fusion surface is indicated by the lines: *a*) Na, *b*) Li, *c*) K, *d*) Rb, *e*) Cs. The surfaces of the other phase transformations are shown by the lines: *f*) Na, *g*) Li, *h*) K, *i*) Rb, *j*) Cs. *k*) Guide lines; *l*) assumed lines.

The range of existence of the phases with a tetragonal structure is occupied by all the lithium and sodium double molybdates. On going to the potassium, rubidium, and caesium compounds, this range (which is bounded below by the surface *8*, *9*, *10*, *11*, *12*, *13*) becomes narrower towards lanthanum and becomes the high-temperature region.

The dependence of the type of structure at low temperatures on $r_{R^{3+}}$ and r_{M^+} can be characterised by the extent to which these radii differ from one another ($\Delta r = |r_{M^+} - r_{R^{3+}}|$) and from the radius of the calcium ion in the scheelite structure [$r_{av} = (r_{M^+} + r_{R^{3+}})/2$]. The greater

this difference, the lower the symmetry of the low-temperature modification (Table 3).

For the potassium, rubidium, and caesium double compounds, the parameter Δr increases towards Lu, whereas r_{av} decreases, that is the two factors act in opposite directions. If the low-temperature potassium and rubidium double molybdates with the $YK(MoO_4)_2$ structure did in fact have orthorhombic symmetry, and not a lower symmetry, r_{av} would obviously have a greater influence on the structure than Δr, since on going towards Lu the symmetry increases to orthorhombic. The fairly large values of Δr, however, have a stronger influence than r_{av}: the heavy rubidium and all the caesium REE molybdates have monoclinic symmetry.

It should also be noted that with increase in the deviation from the "scheelite" radius ratio ($r_{R^{3+}} \simeq r_{M^+} \simeq r_{Ca^{2+}}$) there is an increase in the variety of structural types and in the tendency for polymorphism to be observed (Table 3). As a rule, the symmetry of the high-temperature phase is higher than that of the low-temperature phase. This suggests that with increase in temperature, equalisation of the ion dimensions takes place. Thus it has been shown [49] that the large difference in the ionic radii of Pr and Rb causes these cations to be distributed in separate layers on transformation of the high-temperature modification of $PrRb(MoO_4)_2$ into the low-temperature form.

The high-temperature phase of $LaCs(MoO_4)_2$ has not been identified, and the low-temperature phase is assumed to be tetragonal [31]. It is not excluded, however, that this tetragonal phase is in fact the high-temperature phase, and that the effect on the thermograms at 950° [31] is due merely to partial phase transformation. In this case, $LaCs(MoO_4)_2$ would not be an exception in the diagram (Fig. 1) and would complete the range of tetragonal phases in regular fashion. If this is the case, the low-temperature form of $LaCs(MoO_4)_2$ should have either a monoclinic or an orthorhombic structure, depending on whether it completes the monoclinic range, bounded below by the surface *13*, *17*, *27*, *28*, or the orthorhombic range, bounded on the left by the same surface, and on the right by the surface *29*, *30*, *31*, *32*.

The monoclinic low-temperature modifications of $RRb(MoO_4)_2$, where R = Tm–Lu, and $RCs(MoO_4)_2$, where R = Pr–Lu, have been assigned to the $PrCs(MoO_4)_2$ structural type [31,74]. The X-ray powder diagrams of the caesium molybdates from Pr to Sm can be indexed satisfactorily in the orthorhombic system. The heavier REE show appreciable splitting of some of the lines, which increases with increase in the atomic number of R.

The double tungstates $RM(WO_4)_2$ are characterised by the same regular features as were noted above for the molybdates, but reveal them much more sharply (Table 4).

In fact, the crystals of the NaREE tungstates, as a consequence of the similarity in $r_{R^{3+}}$, r_{M^+}, and $r_{Ca^{2+}}$, have the tetragonal (scheelite) structure and do not exhibit polymorphism, whereas the low-temperature modifications of the lithium double molybdates of the heavy REE have monoclinic symmetry. When heated, they undergo reversible transformations into high-temperature tetragonal phases.

In the case of the scheelite-like lithium double molybdates of the light REE, a polymorphic transformation has been established only for $NdLi(WO_4)_2$ (Table 4). At 665° it gives a weak thermal effect, which is not accompanied by a change in symmetry. Similar transformations can apparently be detected for the other light RLi tungstates.

The decrease in symmetry towards Lu can be attributed to the large contribution of the influence of change in r_{av} compared with Δr. The low-temperature phases of the other double tungstates are monoclinic.

The diagram for the phase transformations of the double tungstates (Fig. 2) is approximately the same as that for the molybdates. Instead of the horizontal surface corresponding to the low-temperature transformations, however, it has a steep sloping surface (*3*, *7*, *8*, *14*, *15*, *16*). In the region where this surface approaches the melting point surface (RK molybdates), the polymorphic transformations are accompanied by marked thermal effects [65] and mechanical stresses leading to breakdown [79]. In the low-temperature region of the surface (RCs tungstates) the transformations correspond to weak effects on the thermograms and do not lead to significant changes in structure.

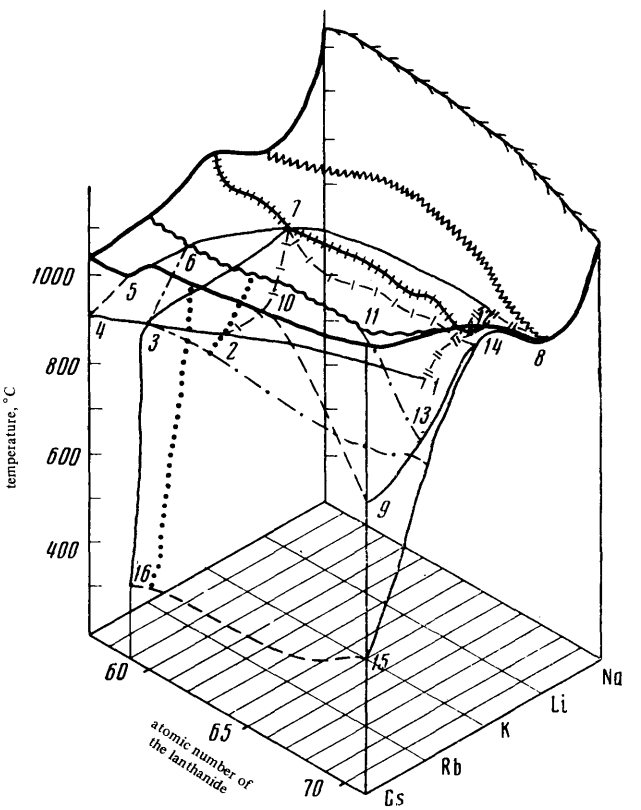


Figure 2. Phase transformations for $RM(WO_4)_2$. For symbols see Fig. 1.

This relationship between the "strength" of a transformation and its proximity to the melting point can be readily followed for other double compounds from all those papers which give DTA curves. On the other hand, it makes it possible to estimate the disruptive tendencies of the phase transformation in the selection of compounds and procedures for the growth of single crystals.

The ranges of existence of the tetragonal and hexagonal modifications are bounded below by the surfaces *1*, *2*, *3*, *4*,

5, *6*, *7*, *8*, and *9*, *10*, *11*, *12*, *13* respectively, and are bounded above by the fusion surface. The reverse order of the positions of Li and Na in Fig. 2 was chosen for the sake of clarity in the representation of the actual diagram as a whole, and also to set off the regular increase in the width of the range corresponding to the tetragonal phases from the caesium double tungstates to the sodium compounds. Although this last feature is not of importance for the double molybdates (since all the phases $RLi(MoO_4)_2$ and $RNa(MoO_4)_2$ are tetragonal), the positions of Li and Na are also represented in Fig. 1, for convenience in comparing the two diagrams. The monoclinic phases lying above and below the sloping surface *3*, *7*, *8*, *14*, *15*, *16* correspond to at least six structural types [15,54,65,74]. Thus as in the case of the molybdates, increase in Δr and r_{av} is accompanied by an increase in the variety of tungstate structures. The symmetry of the high-temperature structure is always higher than that of the low-temperature structure.

It should also be noted that the crystals of the low-temperature forms of the potassium, rubidium, and caesium double tungstates and molybdates exhibit perfect cleavage, and this creates additional difficulties in the growth of large crystals and their use in lasers. The anisotropy of the mechanical properties can be attributed to the tendency for R and M with a large value of Δr to distribute themselves in layers. This increases the degree of order in the structure, however, and hence decreases the width of the luminescence lines, as noted above for the $YK(MoO_4)_2$–Nd^{3+} system.

The existence of "smooth" surfaces on the three-dimensional diagrams giving the phase transformations of $RM(MoO_4)_2$ and $RM(WO_4)_2$, bounding the ranges of existence of related structures, means that we are dealing not with a simple set of compounds, but with systems. This feature makes it possible to represent regularities, to estimate the reliability of published data in those cases where they are contradictory, and to predict various properties which have not yet been established.

IV. FUSION

The "smooth" form of the fusion surfaces on the diagrams (Figs. 1 and 2) makes it possible in many cases to estimate melting points which have not yet been determined: $RNa(MoO_4)_2$ from Nd to Gd ~1160°; $CeNa(MoO_4)_2$ and $PrNa(MoO_4)_2$, apparently, ~1080°; $SmK(MoO_4)_2$ ~ 990°; $GdK(MoO_4)_2$ ~ 960°; $TbRb(MoO_4)_2$ ~ 980°; $TbCs(MoO_4)_2$ ~ 1010°; $CeNa(WO_4)_2$ ~ 1270°; $CeLi(WO_4)_2$ ~ 1060°; and $CeRb(WO_4)_2$ and $CeCs(WO_4)_2$ ~ 1040°.

The melting points of the double tungstates are always higher than those of the corresponding molybdates, so that the high melting points found by Heindl and coworkers [8] for the sodium molybdates of La, Pr, and Nd (Table 5) contradict the values found by other workers [38,58,80].

Data on the fusion of double molybdates and tungstates are contradictory (Tables 6 and 7). It has been suggested [60,61,74] that there exists a boundary of congruent fusion, separating the congruently melting double molybdates and tungstates of the light REE from the incongruently melting double compounds of the heavy REE. For molybdates containing sodium, potassium, and rubidium, this boundary passes through gadolinium or terbium and is then displaced towards the end of the REE series in the case of caesium. For the tungstates it passes through $ErNa(WO_4)_2$, $LaK(WO_4)_2$, $HoRb(WO_4)_2$, and $DyCs(WO_4)_2$. According to other sources [41,65], however, all the compounds $RK(EO_4)_2$ (obtained from solution in a melt) melt congruently.

The suggestion that there is a relationship between the position of the boundary of congruent fusion and the fairly sharp decrease in melting point on going into the range of incongruent fusion, put forward for the rubidium and caesium double tungstates [61], is apparently justified in individual cases. The fusion surface for the double molybdates (Fig. 1) in fact shows a curvature due to a decrease in the melting points along the REE series, beginning at Tb for the rubidium and caesium compounds, at Gd for the potassium compounds, and at Dy for the lithium and sodium compounds, corresponding approximately to the boundary of incongruent fusion (Table 6). The fusion surface of the double tungstates also shows corresponding curvatures in the region of $HoCs(WO_4)_2$, $ErRb(WO_4)_2$, $HoK(WO_4)_2$, $HoLi(WO_4)_2$, and $ErNa(WO_4)_2$. These compounds apparently also form the boundary of incongruent fusion for the tungstates.

Table 6. Temperatures and nature of the fusion of the double molybdates of the REE (R) and alkali metals (M) $RM(MoO_4)_2$*.

R	M				
	Li	Na	K	Rb	Cs
Y	975^{33} 950^{22}	$1110+^{22}$	$980^{22,27}$		
La	930^{33} 1075^{26}	1163^{38} 1140^{58} 1425^{8}	$1070-^{41}$ 1140^{32}	1040^{32} 1020^{31}	980^{32} 1000^{31}
Ce	900^{33}		$930-^{41}$		
Pr	975^{33}	1435^{8}	$1000-^{41}$ 1030^{27}	1015^{44} 1025^{31}	1000^{31}
Nd	1010^{33}	1460^{8}	$990^{-27,41}$	1030^{31}	1010^{31}
Sm	1020^{33}			1015^{31}	1040^{31}
Eu	1025^{33}			1015^{31}	1040^{31}
Gd	1035^{33}		$+51$	1000^{31}	1050^{31-74}
Tb	1020^{33} $1030+^{52}$	$1160+^{52}$	975^{-41+41} $1000+^{52}$		
Dy	1010^{33} 980^{53}	$1090+^{55}$	$975-^{41}$ $+51$	980^{31}	1025^{31}
Ho	1005^{33} $990+^{53}$	$1110+^{55}$	$965-^{41}$ $+51$	1000^{31}	1070^{31}
Er	990^{33+53}	$1100+^{55}$	$955-^{41}$ 990^{27}	1040^{31}	1085^{31}
Tm	950^{33+53}	$1095+^{52}$	$935-^{41}$ $1000+^{52}$	1060^{31}	1115^{31}
Yb	900^{33} $925+^{52}$	$1080+^{52}$	$990-^{41}$ 1025^{52}	1075^{31}	1145^{31}
Lu	835^{33} $863+^{52}$	$1050+^{52}$	$1030-^{41}$ $1050+^{52}$	1100^{31}	1150^{31}

*In Tables 6 and 7, the minus sign denotes congruent fusion, the plus sign denotes incongruent fusion, and the absence of a sign denotes that the nature of the fusion has not been established.

The very sharp decrease in the melting points of the double molybdates formed by cerium with lithium and potassium apparently cannot be related to the nature of the fusion until more information is obtained. The increase in the melting points of the hexagonal high-temperature phases for both the double tungstates and the double molybdates of the heavy REE (Figs. 1 and 2) is evidently not accidental.

The high-temperature modification of $LuK(MoO_4)_2$ should be hexagonal.

In the other cases, the relationship between the melting points and the structures of the high-temperature phases is not so clear.

Table 7. Temperatures and nature of the fusion of the double tungstates of the REE (R) and the alkali metals (M) $RM(WO_4)_2$.*

R	M				
	Li	Na	K	Rb	Cs
Y	1050^{58}	1200^{-60}	$1046^{28,62}$ 1060^{+61}	1070^{+61}	1145^{+61}
La	1040^{58}	$1250^{-60,80}$	1120^{-65} 1160^{-61}	$1050^{54,71}$ 1070^{-61}	$1040^{54,74}$ 1090^{-61}
Ce			1060^{-65}		
Pr	1070^{58}		$1080^{-62,65}$	1020^{54} 1040^{-74}	1050^{57-74}
Nd	1075^{58} 1045^{62}	$1263^{-60,80}$	1075^{-65} 1070^{+61}	1030^{54} 1045^{74} 1055^{-61}	1080^{54} 1100^{74} 1055^{-61}
Sm	1120^{58}	1250^{-60}	1060^{-65} 1030^{+61}	$1050^{54,74}$ 1080^{-61}	1100^{54} 1060^{74} 1100^{-61}
Eu	1130^{58}	1248^{-60}	1065^{-65} 1052^{+61}	$1070^{54,74}$ 1095^{-61}	1100^{54} 1065^{74} 1135^{-61}
Gd	1135^{58}	1260^{-60} 1253^{-60}	1075^{-65} 1060^{+61}	1070^{54} 1075^{74} 1105^{-61}	1100^{54} 1075^{74} 1162^{-61}
Tb	1120^{58}		1080^{-65} 1070^{+61}	1070^{54} 1075^{74} 1105^{-61}	1100^{54} 1080^{74} 1165^{-61}
Dy	1108^{58}	1230^{-60}	1075^{-65} 1070^{+61}	1070^{54} 1080^{74} 1120^{-61}	1100^{54} 1075^{74} 1140^{-61}
Ho	1086^{58}	1215^{-60}	1070^{-65} 1075^{+61}	1070^{54} 1075^{74} 1085^{-61}	1080^{54} 1090^{74} 1155^{+61}
Er	1069^{58}	1200^{-60}	1080^{-65} 1070^{+61}	1060^{54} 1070^{+74} 1075^{+61}	1100^{54} 1110^{+74} 1145^{+61}
Tm	1008^{58}	1175^{+60}	1055^{-65}	1080^{54} 1090^{74}	1120^{54} 1120^{74}
Yb	982^{58+76}	1160^{+60}	1045^{-65} 1090^{+61}	1100^{54} 1105^{74} 1130^{+61}	1150^{54} 1140^{74} 1260^{+61}
Lu	975^{58}	1134^{+60}	1090^{-65}	1130^{54} 1150^{74}	1180^{54} 1150^{74}

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Almost all compounds of the type $RM(EO_4)_2$, where R = the REE and Y, M = an alkali metal, and E = Mo or W, have been prepared, but only a few of them have been obtained in the form of large crystals.

Single crystals of double tungstates and molybdates containing REE exhibit valuable laser properties. Their luminescence characteristics depend on the ratio of the dimensions of the R^{3+} and M^+ ions and on the structure. The low-temperature structure of $RM(EO_4)_2$ is determined chiefly by the quantities $\Delta r = |r_{M^+} - r_{R^{3+}}|$ and $r_{av} = (r_{M^+} + r_{R^{3+}})/2$, which characterise the extent of the departure from the scheelite radius ratio of the ions $r_{M^+} \simeq r_{R^{3+}} \simeq r_{Ca^{2+}}$. With increase in Δr and r_{av}, the symmetry of the low-temperature modification decreases, the number of structural types increases, the tendency to exhibit polymorphism becomes greater, and the R and M atoms tend to distribute themselves in individual layers, leading to the production of perfect cleavage in the crystals. At the same time, increase in these two parameters leads to a decrease in the disorder of the low-temperature structure and a corresponding decrease in the width of the luminescence line.

Δr and r_{av} change in opposite directions along the REE series, so that in some cases the symmetry of the low-temperature phase increases towards lutetium.

The symmetry of the high-temperature modification is never lower than that of the low-temperature phase.

The formation of a given modification depends on the method of preparation and the subsequent thermal treatment. This constitutes the chief difficulty in the deduction of the above regular features from an analysis of published material.

The construction of phase transformation diagrams on the basis of published data has made it possible to compile a fairly complete picture of the polymorphism and fusion of the rare earth metal double tungstates and molybdates, to reveal the regions with identical symmetries, and in some cases to estimate the structures, melting points, and polymorphic transitions where these have not yet been established.

A relationship evidently exists between the nature of the fusion and the form of the fusion surface; the boundary of incongruent fusion passes in "steps" over this surface.

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Mendeleev Institute of
Chemical Technology,
Moscow

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Advances in Electronic Raman Spectroscopy of the Lanthanides†

J.A.Koningstein

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I. INTRODUCTION

Since the discovery of Raman scattering (RS), many investigators based their explanation of the characteristics of the spectra of solids, liquids, and gases on Placzek's work. Despite the fact that the first studies on Raman scattering were carried out by physicists, during the period from 1935 until the introduction of the laser, this type of spectroscopy has been used extensively by chemists as a means of establishing molecular structures. The vibrational and rotational Raman spectra have been almost always excited by a low-pressure mercury lamp which precluded a direct comparison of specific experimental data with theory. For example, it was difficult to obtain information about the individual elements of the scattering tensor, since the direction of propagation of the exciting radiation was not exactly parallel or perpendicular to the direction of the observation of the scattered radiation. The measured degrees of depolarisation of the Raman lines of liquids and gases almost always differed from the theoretical values, so that the calculation of the degrees of depolarisation of vibrations of a particular type or the *a priori* calculation of absolute intensities constituted a cumbersome procedure.

Most of the experimental studies during the above period dealt with the excitation of Raman transitions in the vibrational or rotational molecular levels. All these levels are linked to the electronic ground state of the molecule. Electronic Raman scattering was observed only for the NO molecule[1]. In 1932 Rasetti attributed the 121 cm^{-1} Raman line for this molecule to the $^2\Pi_{1/2}-{}^2\Pi_{3/2}$ transition. According to Gerding's evidence, Gorter undertook experiments with lanthanide ions during the second world war and it was not until 1964 that Hougen and Singh[3] succeeded in exciting Raman scattering in the electronic transitions of Pr^{3+} in $PrCl_3$. Immediately before the publication of this paper, Elliott and Loudon[4] predicted the possibility of observing electronic Raman scattering by lanthanide ions. In addition, Chau observed Raman scattering for Ce^{3+} in $CaWO_4$.[5] In all the experiments the mercury lamp still served as the light source and photographic plates were used to record the spectra. Very little information was obtained about the intensity of this effect relative to the intensities of strong Raman lines for certain well known liquids.

† This is an English translation of the review published by the author in Russian (Ed. of Translation).

Placzek pointed out that the scattering tensor for electronic transitions differs from the scattering tensor for vibrational and rotational transitions[6,9]. In the latter case the tensor is symmetric, whereas the tensor for electronic transitions may become antisymmetric.

Numerous crystalline compounds containing lanthanide ions are now available and, when it is necessary to separate the phonon Raman spectrum from electronic effects, the elements of the scattering tensor must be investigated.

In 1966 the author of the present review began a programme devoted to the excitation of electronic Raman scattering of lanthanide ions in certain crystals using the radiation from a helium–neon laser at 6328 Å. By that time it became clear that the individual elements of the Raman scattering tensor for vibrational transitions can be measured and there was hope that measurements of this type might be carried out also for electronic transitions. The helium–neon laser was chosen because, as can be seen from the energy level diagram for lanthanide ions, only a few of them have excited states with energies equal to those of the laser emission (Fig. 1). By employing a more sensitive recording system, the author succeeded in 1966 in exciting the Raman spectra of tervalent lanthanide ions in the lattice of the yttrium–gallium garnet[6,7]; this was followed by a series of experiments on the same ions in other crystals[8–12].

In Placzek's theory of polarisability for vibrational Raman scattering, attention was concentrated on the polarisability of the molecular ground state and the role of the intermediate states was to a considerable degree limited. The matrix elements of the electrical dipole moment operator for transitions between the ground and intermediate states appear in the expressions for the elements of the scattering tensor. In the general case, our knowledge of the wave functions for these states is insufficient to calculate the matrix elements and hence we have also to calculate the elements of the scattering tensor for vibrational transitions. The situation is almost completely different for tervalent lanthanide ions. The wave functions for the states of the lanthanide ions—free or in an environment of specified symmetry—have been calculated and Axe[13] used these wave functions in the calculation of the absolute Raman intensities in the electronic transitions of certain lanthanide ions. In these calculations the effect of the antisymmetry of the scattering tensor was neglected.

However, Mortensen and the present author[14] showed that a large contribution by antisymmetric tensors to the total intensities may be expected from many ions. Indeed,

in certain cases the contribution from antisymmetric tensors is greater than that from symmetrical tensors and at least one case has been found where the Raman transitions are due to a completely antisymmetric tensor[9]. Apart from the absolute intensities, the ratio of the intensity of Rayleigh scattering to the intensity of electronic Raman scattering of all the lanthanides has also been calculated[15] and in subsequent reports a relation was established between the force and symmetry of the crystal field on the one hand and the polarisation characteristics of the complete electronic Raman spectra on the other[16,17].

Following the appearance of the argon and krypton ionic lasers towards the end of 1970, more detailed experimental data were obtained[18] and electronic Raman scattering was observed for all lanthanide ions with two exceptions[19,20]. The experimental results confirmed the theoretical prediction that the intensity of the electronic Raman lines is lower than the intensity of scattering by the crystal matrix phonons. It was also noted that the intensities depend greatly on the electronic configuration of the ions. However, the contribution of antisymmetric tensors to the intensity is less marked, with the exception of the Eu^{3+} ion, where the scattering is entirely due to the antisymmetric tensor[21]. The appearance of this tensor is unique in physics and chemistry and in Raman spectroscopy is a result of profound changes in selection rules.

A glance at the energy level diagrams (Fig. 1) shows that many levels have been designated by the quantum number J which is a multiple of 1/2. This implies that representations of binary groups must be used for the investigation of the symmetry of the levels in the crystal field and of the scattering tensor components. The main result is that the tensors for electronic and vibrational transitions are completely different in all the crystals[22].

We shall conclude the introduction with general remarks concerning the selection rules for Raman scattering[23]. All the states arising from the same electronic configuration have the same parity—they are either even or odd. The scattering operator $\hat{\alpha}_{\rho\sigma}$ (where ρ and $\sigma = x, y, z$) is an even operator and the integral $\int \Psi_n \hat{\alpha}_{\rho\sigma} \Psi_m d\tau \neq 0$, where Ψ_n and Ψ_m are the wave functions of these states. Thus, like vibrational and rotational scattering, electronic scattering is formally allowed.

II. VIBRATIONAL AND ELECTRONIC RAMAN SCATTERING[14,15]

We shall suppose that a photon flux is incident on atoms, molecules, or a crystal. Most of these photons will not interact with the species but some of them (less than 1%) will be involved in an elastic interaction. The frequency of the electromagnetic radiation then remains unchanged and the elastic interaction leads to the so-called Rayleigh scattering. However, a much smaller number of protons are scattered inelastically. An atom, ion, or molecule may be excited from the ground to the first or second excited state and, when this has happened, the law of conservation of energy shows directly that the scattered photons have an energy and consequently a frequency differing somewhat from that of the incident photons. It is of course also possible that a species can return from the excited to the ground state, whereupon the [liberated] energy is added to the energy of the incident photons, which leads to a decrease of the wavelength of the scattered radiation. Thus the Raman spectrum appears in the form of emission lines corresponding to greater and smaller energies than the undisplaced Rayleigh scattering lines. Since in the excited states there are fewer species than in the ground state, the intensity of the so called anti-Stokes Raman lines is lower than of the Stokes Raman lines. The intensity ratio of these lines is specified by the Boltzmann distribution law. However, in order to obtain a clear description of the Raman intensity, it is necessary to examine this process in greater detail.

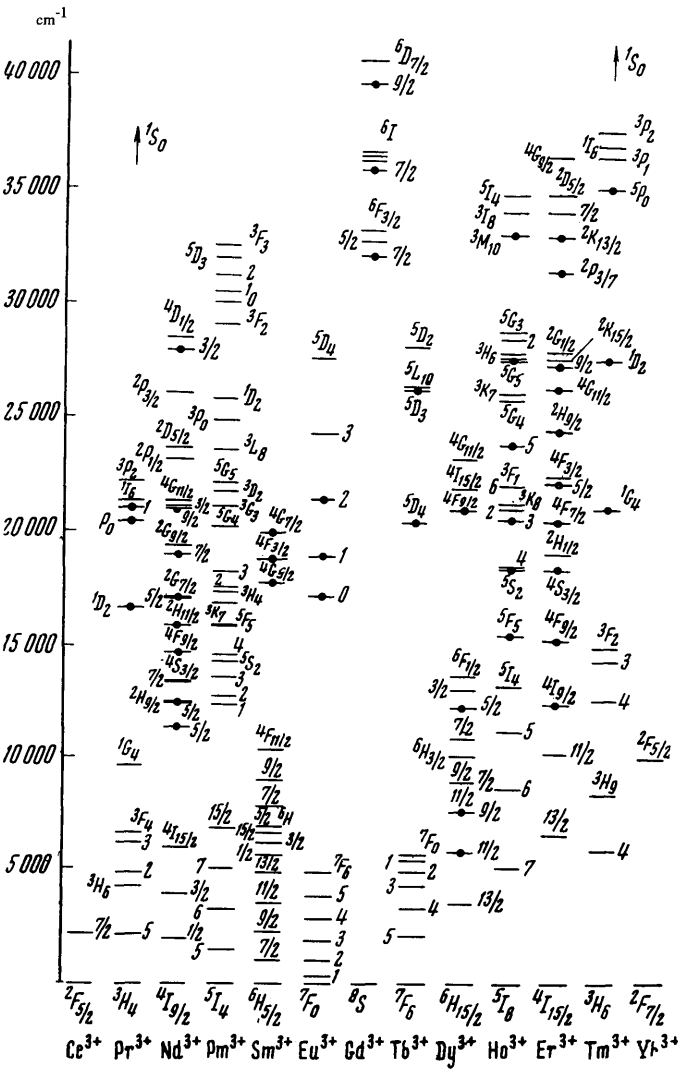


Figure 1. Energy level diagrams for tervalent lanthanide ions. The emission energy of the He—Ne and Ar^+ lasers is between 15 000 and 22 000 cm^{-1}. Certain lanthanide ions absorb this radiation with a consequent appearance of fluorescence, which precludes the observation of electronic Raman scattering.

Fig. 2 represents the case where the incident radiation is propagated along one of the axes of the rectangular coordinate system and the scattered radiation is observed in

the direction perpendicular to that of the propagation of the incident light rays. We shall suppose that at the origin of the rectangular coordinate system there is a single crystal with cubic symmetry and that its macroscopic axes coincide with the x, y, and z axes of the coordinate system. The electric field of the incident wave may induce a dipole moment in the atom or molecule of the crystal. In the general case, the direction of this induced moment will not be parallel to the electric vector of the incident wave. Raman scattering may be described by the tensor

$$\mu^i = (\alpha)\, E,$$

where

$$\begin{aligned} \mu_x^i &= \alpha_{xx}E_x + \alpha_{xy}E_y + \alpha_{xz}E_z, \\ \mu_y^i &= \alpha_{yx}E_x + \alpha_{yy}E_y + \alpha_{yz}E_z, \\ \mu_z^i &= \alpha_{zx}E_x + \alpha_{zy}E_y + \alpha_{zz}E_z. \end{aligned} \qquad (1)$$

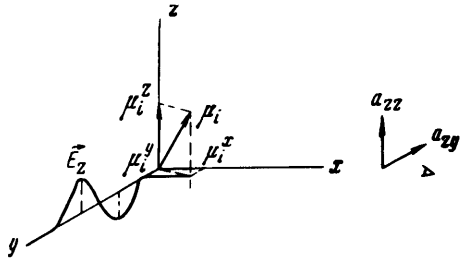


Figure 2. Raman scattering in a cubic crystal the a, b, and c axes of which are parallel to the axes of the cartesian coordinate system. The laser radiation enters the crystal in the direction of the y axis and the scattered Raman radiation is observed along the x axis. The induced dipole moment μ_i and its components μ_i^z, μ_i^y, and μ_i^x are shown. By placing an analyser in front of the monochromator, it is possible to resolve the α_{zz} and α_{zy} components. They appear in the $y(zz)x$ and $y(zy)x$ polarisation Raman spectra.

In each specific case different components of the scattering tensor can be determined by a suitable choice of direction of the polarisation of the incident radiation, the crystal orientation, and the direction of observation of the scattered radiation. Hitherto, we have not discussed the types of Raman scattering. Raman spectroscopy has proved to be a very successful method for the determination of molecular structures in the gas phase, in liquids, and crystals using rotational or vibrational spectra.

The induced moment for vibrational Raman scattering is the transition moment between the ground and excited vibrational states. In order to relate the intensity of the Raman line to the elements of the scattering tensor, the polarisability of the molecule in the ground state $(\alpha_{\rho\sigma})$ is formulated in the form of an expansion in terms of the coordinates of the normal vibrations of the molecule. The intensity of the Raman lines is related to the derivatives of the polarisability[24] of the molecule in the ground state with respect to the normal coordinates (Q). Recently another model was proposed[25] for vibrational Raman scattering. The following expression, obtained for the components of the scattering tensor $(\alpha_{\rho\sigma})_{kn}$ (where ρ and $\sigma = x, y, z$), was used for the transition between the states k and n of the system:

$$(\alpha_{\rho\sigma})_{kn} = h^{-1}\sum_r \frac{\langle n|e\sigma|r\rangle\langle r|e\rho|k\rangle}{\nu_0 - \nu_{kn}} + \frac{[\rho \leftrightarrow \sigma]}{\nu_0 + \nu_{kn}}. \qquad (2)$$

The subscripts k and n in Eqn. (2) show that Raman scattering begins from the state k and terminates at the state n, ν_0 is the frequency of the incident light, $\langle n|e\sigma|r\rangle$ is a matrix element of the electric dipole moment, and the summation with respect to r is carried out over all the excited states of the system. The electric dipole moment can be formulated as follows:

$$\int \Psi_n^* e\sigma \Psi_r d\tau.$$

In the general case, the wave function Ψ_n is defined as the product of the electronic wave function $\Psi_n(\mathbf{r}Q)$ and the vibrational wave function $\varphi_v(Q)$, where n is the electronic quantum number, v the vibrational quantum number, and Q the normal coordinate. The electronic motions may be sensitive to the motions of the nuclei in the molecule. Assuming that this interaction is weak, the following form may be used for the Hamiltonian $\mathcal{H}$:

$$\mathcal{H} = \mathcal{H}_0 + \left(\frac{\partial \mathcal{H}}{\partial Q}\right)_{Q=0} Q + \ldots$$

and the wave function

$$\begin{aligned} \Psi_n(\mathbf{r}, Q) &= \Psi_n^0(\mathbf{r}, Q=0) + \\ &+ \sum_{l\neq n} \frac{\int \Psi_l^0(\mathbf{r}, Q=0)\left(\frac{\partial \mathcal{H}}{\partial Q}\right)_{Q=0} \Psi_n^0(\mathbf{r}, Q=0)\, Q d\tau}{E_l^0 - E_n^0} \Psi_l^0(\mathbf{r}, Q=0), \end{aligned} \qquad (3)$$

where $\mathcal{H}_0$ is the Hamiltonian of the vibrating molecule in the equilibrium configuration and E_l^0 is the energy of the first excited electronic state of the molecule.

The electronic wave functions in the form of a series [Eqn. (3)] can now be substituted in the expression for the matrix elements of the electric dipole moment, which enters into the component of the scattering tensor in Eqn. (1). Fortunately, it is possible to make certain simplifications and to obtain the following relations.

I. Electronic Raman scattering $(n;\ v = 0 \rightarrow k;\ v = 0)$:

$$(\alpha_{\rho\sigma})_{nv=0;kv=0} = h^{-1}\sum_r \left\{ \frac{(M_\rho)_{nr}(M_\sigma)_{rk}}{\nu_{rk} - \nu_0} + \frac{[\rho \rightarrow \sigma]}{\nu_{rn} + \nu_0} \right\}. \qquad (4a)$$

II. Vibronic Raman scattering $(n;\ v \rightarrow k;\ v')$:

$$(\alpha_{\rho\sigma})_{nv;kv'} = h^{-1}\langle \varphi_{v'}|Q|\varphi_v\rangle \sum_r \left\{ \frac{(M_\rho)_{kr}[(M_\sigma)_{rl}h_{ln}^Q + (M_\rho)_{ln}h_{lr}^{Q*}]}{\nu_{rk} - \nu_0} + \ldots \right\}. \qquad (4b)$$

The constant h_{ln}^Q is defined by the integral

$$\int \Psi_l^0(\mathbf{r}, Q=0)\,(\partial\mathcal{H}/\partial Q)_{Q=0}\Psi_n^0(\mathbf{r}, Q=0)\, d\tau/(E_l^0 - E_n^0).$$

If the vibronic interaction is weak, it follows automatically that the constants h_{ln}^Q are small. As a result, we find that the main contribution to the intensity of electronic Raman scattering levels comes from the elements of the scattering tensor $(\alpha_{\rho\sigma})_n$; $v = 0 \rightarrow k$; $v = 0$. Vibronic Raman scattering is probably insignificant compared with the more intense electronic Raman scattering in the transition between the states k and n.

It is interesting to replace the quantum number n by k in Eqns. (4a) and (4b). The first of these equations becomes identical with the expression for Rayleigh light

scattering. The replacement of n by k in Eqn. (4b) leads to the relation

$$(\alpha_{\rho\sigma})_{nv;nv'} = \hbar^{-1}\langle\varphi_{v'}|Q|\varphi_v\rangle \sum_r \left\{\frac{(M_\rho)_{nr}[(M_\sigma)_{rl}h^Q_{ln} + (M_\rho)_{ln}h^{*Q}_{lr}]}{\nu_{rn}-\nu_0} + \ldots\right\}, \quad (5)$$

which gives the elements of the Raman scattering tensor for the transition between the vibrational levels v and v' linked to the same ground electronic state n. Thus vibrational Raman scattering has now been described in terms of a model where interaction with vibrations has been introduced. This model, incorporating vibronic interactions, was proposed, as already stated, by Albrecht[25], who also showed that the selection rules for Raman scattering may be obtained by examining the conditions under which the constants h^Q_{nl} and h^Q_{lk} are not zero.

Eqns. (4a) and (5) may be used directly to investigate the symmetry of the scattering tensor. The tensor is symmetric if the element $(\alpha_{\rho\sigma})_{nk}$ is equal to the element $(\alpha_{\sigma\rho})_{nk}$. For vibrational Raman scattering levels, the tensor is symmetric, but for electronic Raman scattering it is found that this condition is not obligatory. One should probably note here that the antisymmetry of the scattering tensor at vibrational levels can also obtain if (a) the wave function entering into the matrix elements of the electric dipole moment operator are not real or (b) the electronic ground state of the molecule is degenerate. The vibrational model loses validity for a degenerate ground state and the considerations employed to obtain expressions for a non-degenerate ground state are inapplicable in this instance.

The transition between the states k and n is allowed in Raman scattering if the matrix element $\langle k|\hat{\alpha}_{\rho\sigma}|n\rangle \neq 0$. The operator $\hat{\alpha}_{\rho\sigma}$ can be formulated as follows:

$$(\hat{\alpha}_{\rho\sigma})_{kn} = \sum_r \frac{|e\sigma|r\rangle\langle r|e\rho|}{\nu_0 - \nu_{kn}} + \frac{[\rho\rightarrow\sigma]}{\nu_0 + \nu_{kn}}. \quad (6)$$

In order to find the conditions under which the matrix element does not become zero, it is necessary to know the transformation properties of the wave functions of the states k and n and the symmetry properties of the scattering tensor itself. The matrix element does not become zero if the direct product of the irreducible representations of the wave functions of k and n and the tensor contains a fully symmetric representation of the point groups. The symmetry properties of the electronic levels may be obtained, for example, from crystal field calculations. The transformation properties of the elements of the scattering tensor are sometimes quoted in the tables of characters of various point groups. However, these data refer only to the special case of vibrational or rotational Raman scattering and above it was shown that in this case the tensor is symmetric. Thus the question arises of what changes occur in the transformation properties when the tensor becomes antisymmetric.

III. THE RAMAN SCATTERING TENSOR

The transformation properties of the antisymmetric part of the scattering tensor are specified by the symmetry of the $\alpha_{\rho\sigma} - \alpha_{\sigma\rho}$ (σ, $\rho = x, y, z$) combinations. The transformation properties of these combinations are not quoted directly in the tables of characters of various point groups. It can be shown that the antisymmetric combinations for all rotations transform as an ordinary vector, and in inversion the transformation is more as an axial vector than a polar vector. This is also valid for the transformation properties of the rotations about the axes of the cartesian coordinate system (R_Z, R_Y, and R_X), so that the transformation properties of the transformation of the antisymmetric part of the scattering tensor and of the rotations about R_Z, R_Y, and R_X are analogous. They can be found directly from the character tables, for example those quoted by Wilson et al.[26]

Ions in crystals occupy positions with specific symmetry. Thus the components of the tensor and the wave functions of the electronic levels may be designated in accordance with the representation of the known point groups. However, the angular components of the electronic wave functions are formulated in terms of the polar coordinates r, θ, and φ, while the symmetry of the tensor was considered above in terms of cartesian coordinates.

The intensity of Raman scattering in an electronic transition is proportional to the square of the matrix element $\langle n|\hat{\alpha}_{\rho\sigma}|m\rangle$, but the n and m wave functions of the operator $\hat{\alpha}_{\rho\sigma}$ have still not been defined in terms of the same coordinate system.

The tensor $(\alpha_{\rho\sigma})$ can be transformed into one in terms of spherical coordinates. These new tensors are irreducible and their components are designated by α^K_Q. The difference between the cartesian and irreducible tensors is that the components of the latter can be combined into three separate sets. In an arbitrary rotation, the members of each set are transformed into one another (or into their combinations), which does not happen for the components of the tensor in terms of cartesian coordinates. The relation between $\alpha_{\rho\sigma}$ and α^K_Q is indicated in Table 1.

Table 1. Relation between the components of the tensor in the cartesian coordinate system and the components of irreducible tensors.

$\alpha^0_0 = -(1/\sqrt{3})(\alpha_{xx}+\alpha_{yy}+\alpha_{zz})$,	$\alpha^2_2 = \frac{1}{2}(\alpha_{xx}-\alpha_{yy}+i\alpha_{xy}+i\alpha_{yx})$,
$\alpha^1_1 = \frac{1}{2}(-\alpha_{xz}+\alpha_{zx}-i\alpha_{yz}+i\alpha_{zy})$,	$\alpha^2_1 = -\frac{1}{1}(\alpha_{xz}+\alpha_{zx}+i\alpha_{yz}+i\alpha_{zy})$,
$\alpha^1_0 = (1/\sqrt{2})(i\alpha_{xy}-i\alpha_{yz})$,	$\alpha^2_0 = (1/\sqrt{6})(2\alpha_{zz}-\alpha_{xx}-\alpha_{yy})$,
$\alpha^1_{-1} = -\frac{1}{2}(\alpha_{xz}-\alpha_{zx}-i\alpha_{yz}+i\alpha_{zy})$,	$\alpha^2_{-1} = \frac{1}{2}(\alpha_{xz}+\alpha_{zx}-i\alpha_{yz}-i\alpha_{zy})$,
	$\alpha^2_{-2} = \frac{1}{2}(\alpha_{xx}-\alpha_{yy}-i\alpha_{xy}-i\alpha_{yx})$.

It is useful to compare the three sets of irreducible tensor components and the s, p, and d orbitals defined in terms of polar coordinates. Like the s orbitals, the irreducible tensor component α^0_0 is completely invariant for all rotations, while the $\alpha^1_{1,0,-1}$ components are mainly transformed like the p orbitals: p_X, p_Y, and p_Z. However, there is a small difference: the orbitals change sign following the inversion of the coordinate system, while the tensor components are invariant in this operation. There is also an analogy between the transformation properties of the d orbitals and the five α^2_Q components ($Q = 2, 1, 0, -1, -2$).

Suppose, for example, that an electronic Raman transition has been induced between the states ^1S and ^3P with the electronic configuration $(p)^2$. We assume that an atom or ion is located in the crystal in a position where

the symmetry is very high, for example O_h. A necessary condition for the Raman scattering in the electronic transition to be allowed is that the fully symmetric representation of the point group is contained in the direct product of the representations:

$$\Gamma_i \times \Gamma_{\alpha_Q^K} \times \Gamma_i .$$

The state (i), which is the lowest in Raman scattering, transforms as the fully symmetric representation of the point group and it is therefore seen that the non-zero components of the scattering tensor transform as the representation to which the finite state p belongs. This finite state is a spectroscopic P state ($l = 1$) and the non-zero components of the scattering tensor α_Q^K are those which transform as the p orbitals. The α_Q^1 components constitute the antisymmetric part of the scattering tensor (see Table 1); Raman scattering in the transition between these states is related to the scattering tensor, which is partly asymmetric. The components of the irreducible tensors may be used not only to establish the selection rules but also they are important for the calculation of the absolute Raman intensities.

In translational Raman scattering, such calculation is very difficult, since in the expression for the tensor element [Eqn. (1)] it is necessary to carry out a summation over all the states r of the system. For electronic Raman scattering, these states are purely electronic and not vibrational, which simplifies the calculations. If the average frequency $\tilde{\nu}_{\chi k}$ is determined by the centre of gravity of the energy $h\tilde{\nu}_{\chi k}$ of one specific excited configuration, the denominator in Eqn. (1) becomes

$$(\nu_{kr} - \nu_0)^{-1} = (\tilde{\nu}_{\chi k} - \nu_0)^{-1}(1 + x + x^2 + \ldots), \qquad (7)$$

where

$$x = (\tilde{\nu}_{\chi k} - \nu_{rk})/(\tilde{\nu}_{\chi k} - \nu_0).$$

The $4f-5d$ transition in Ce^{3+} has a frequency of about 50 000 cm^{-1}. If the Raman spectra are excited by light with a frequency $\nu_0 = 20\,000\ cm^{-1}$, then $x > 1$, since all the states r have almost the same energy. Moreover, the frequency dependence of the summation is now found from the terms ν_{rk}, where r are the states of an individual electronic configuration.

We now have

$$\langle r|[\mathcal{H}\sigma]|k\rangle = \langle \mathcal{H}r|\sigma|k\rangle - \langle r|\sigma\mathcal{H}|k\rangle = (\nu_{rk}/h)\langle r|\sigma|k\rangle \quad , \qquad (8)$$

where $\mathcal{H}$ is the Hamiltonian of the system and σ is the electric dipole moment of the operator. Combination of Eqns. (7) and (8) with Eqn. (4a) yields

$$(\alpha_{\rho\sigma})_{kn} \approx \sum_r \frac{1}{h}\frac{\tilde{\nu}_{\chi k}\langle n|\rho|r\rangle\langle r|[\mathcal{H}\sigma]|k\rangle}{\tilde{\nu}_{\chi k} - \nu_0} + \frac{\tilde{\nu}_{\chi n}\langle n|[\mathcal{H}\sigma]|r\rangle\langle r|\rho|k\rangle}{\tilde{\nu}_{\chi n} + \nu_0} . \qquad (9)$$

If the Raman intensity is now specified by the integral $\langle k|\hat{\alpha}_{\rho\sigma}|n\rangle$ then the operator $\hat{\alpha}_{\rho\sigma}$ becomes

$$\hat{\alpha}_{\rho\sigma} \simeq \sum_r \frac{\tilde{\nu}_{\chi k}\{|\rho|r\rangle\langle r|[\mathcal{H}\sigma]|\}}{\tilde{\nu}_{\chi k} - \nu_0} + \frac{\nu_{\chi n}\{|[\mathcal{H}\sigma]r\rangle\langle r|\rho|\}}{\tilde{\nu}_{\chi n} + \nu_0} . \qquad (10)$$

The wave functions $|r\rangle$ and $|n\rangle$ of tervalent ions are in the general case characterised by the quantum numbers $nLSJJ_Z$. Under the influence of the crystal field, the LSJ sets split into $2J + 1$ components, as a result of which the states of the crystal field are no longer pure J_Z substates but represent a mixture of J_Z substates resembling that formulated below:

$$|\Psi\rangle = a_{nLSJJ_z}|J, J_z\rangle + a_{nLSJJ'_z}|J, J'_z\rangle + \ldots + a_{nLSJ-J_z}|J, -J_z\rangle \qquad (11)$$
$$\rangle \sum_{J_z} a^2_{nLSJJ_z} = 1.$$

If the coefficients a are introduced into Eqns. (9) or (10), then the single summation with respect to the states r assumes the following form:

$$\sum_{nLSJJ_z}\sum_{nLSJJ'_z}\sum_{n''L''S''J''J''_z} a(nLSJJ_z)\, a(nLSJJ'_z)\, a(n''L''S''J''J''_z) , \qquad (12)$$

where all the wave functions have been normalised. Consequently, similarly to Eqn. (11), we have

$$\sum_{J_z \in \chi} a^2(n''L''S''J''J''_z) = 1. \qquad (13)$$

We can now introduce the components of the irreducible tensors and employ Judd's sums rule, since two operators $\hat{\rho}$ and $[\mathcal{H}\sigma]$ appear in the operator $\hat{\alpha}_{\rho\sigma}$ [Eqn. (10)]. We obtain the following final expression for the element α_Q^K:

$$\hat{\alpha}'^K_{knp} = \sum_{\nu SLJM}\sum_{\nu' SL'J'M'} a^*(n;\gamma'SL'J'M')\, a(k;\gamma SLM)\langle\gamma'SL'J'M'|U^K_Q|\gamma SLJM\rangle + \\ + \sum_\chi\left[\sum_{i=0}^{p}\binom{p}{i}\left(-\frac{1}{h}\right)^i\left\{\frac{(\tilde{\nu}_{\chi k})^{p-i}}{(\tilde{\nu}_{\chi k} - \nu)^{p+1}}(nl\|r\|n'l')(n'l'\|[\mathcal{H}^i r]\|nl)\times\right.\right. \\ \left.\left.\times(-1)^i\frac{(\tilde{\nu}_{\chi n})^{p-i}}{(\tilde{\nu}_{\chi n} + \nu)^{p+1}}(-1)^K(nl\|[\mathcal{H}^i r]\|n'l')(n'l'\|r\|nl)\right\}\right]\times \\ \times(2K+1)^{1/2}\begin{Bmatrix} 1 & K & 1 \\ l & l' & l\end{Bmatrix}(-1)^K \qquad (14)$$

and for the matrix element

$$\langle\gamma'SL'J'M'|U^K_Q|\gamma SLJM\rangle = (-1)^{J'-M'}\begin{pmatrix} J' & K & J \\ -M' & Q & M\end{pmatrix}\times \\ \times\langle\gamma'SL'J'\|U^K\|\gamma SLJ\rangle \quad . \qquad (15)$$

Raman scattering has now been formulated for transitions between the crystal field states $|SLJJ_Z\rangle$ and $|SL'J'J'_Z\rangle$; here

$$(nl|r|n'l') = \int R_{nl}(r)\, R_{n'l'}\, d\tau \quad .$$

$|n'l'\rangle$ are wave functions for the excited configuration. The values of the matrix elements $\langle n'SL'\|U^K\|nSL\rangle$ have been published by Nielson and Koster[27].

One can gain a better understanding of the essential feature of the selection rules for Raman scattering from the knowledge of the conditions under which the j-symbol is non-zero:

$$\begin{pmatrix} J' & K & J \\ -J'_z & Q & J_z\end{pmatrix} \quad . \qquad (16)$$

The $3j$-symbol is automatically zero if $-J'_Z + Q + J_Z$ and $J' + K + J$ do not simultaneously satisfy the usual triangle conditions (for $J = 0$, this implies that $J' = K$). The selection rules with respect to J are $\Delta J \leq 2$ and also $\Delta S = 0$ and $\Delta L \leq 2$. Thus the additional conditions in the calculation of the scattering tensor are as follows: (a) expansion (7) must be valid and (b) all the states involved in Raman scattering must be those of the crystal field and not the ligand field.

IV. INTENSITY OF RAMAN SCATTERING AND THE CRYSTAL FIELD

Having an expression for α_Q^K, it is possible to calculate the ratios $\alpha_0^0/(\alpha_Q^1 + \alpha_Q^2)$ and α_Q^1/α_Q^2. The first represents the ratio of the intensities of Rayleigh and Raman scattering and the second the ratio of the antisymmetric and symmetrical parts of the Raman scattering tensor. Fig. 3 presents the Rayleigh and Raman intensity ratios for all the lanthanides where there is a transition between

the lowest and subsequent manifold LSJ states of the free ions. These manifold states for Ce, Pr, Nd, Sm, Eu, Tb, and Dy have an energy greater by 2500 cm^{-1} than that of the ground state, while for Tm and Yb the energy is greater by 10000 cm^{-1}. In the general case, the ratio is between 10^2 and 10^3, i.e. approximately the same as for Raman scattering in vibrational transitions.

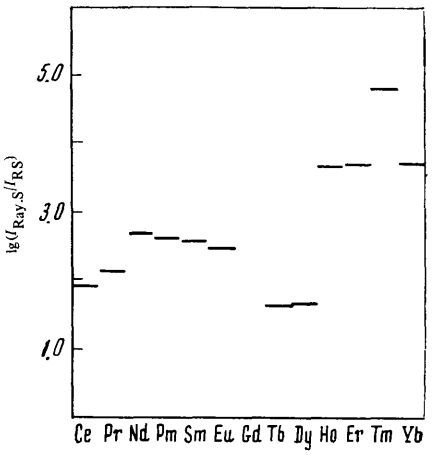


Figure 3. The ratio of the Rayleigh and electronic Raman scattering intensities of tervalent lanthanide ions. The Raman scattering takes place between the set of levels of the ground state and the first higher set of levels. For Yb^{3+}, the difference between the energies of these levels is about 10000 cm^{-1}, which accounts for the higher Rayleigh and Raman intensity ratio, since the intensity of the Raman lines (Stokes lines) is proportional to $(\nu_0 - \nu_{kn})^4$.

Table 2 lists the scattering cross-sections for certain electronic effects. The absolute value of 10^{-32} cm^2 for electronic scattering may be compared with 10^{-28} cm^2 [the experimental value for the $\nu_1(C_6H_6)$ line at 992 cm^{-1}] for vibrational Raman scattering[28]. Thus the intensity of the electronic transitions is lower than that of the majority of the vibrational Raman bands. The fact that one cannot neglect the antisymmetry of the scattering tensor becomes evident when the theoretical results in Fig. 4 are compared. The degree of antisymmetry diminishes if the transition is between states with different values of J; however, lanthanide ions with less than seven f electrons show a higher degree of antisymmetry. It was shown in Section III that the transition associated with the $\alpha_{\rho\sigma} - \alpha_{\sigma\rho}$ ($\alpha_Q{}^1S$) tensor combination is possible only for electronic Raman scattering.

Table 2. Absolute cross-sections[a] of Rayleigh and electronic Raman scattering of Pr^{3+} and Tm^{3+} ions.

Ions	Rayleigh scattering, cm^2	Raman scattering	Transition in Raman scattering
Pr^{3+}	$0.9\cdot10^{-29}$	$0.6\cdot10^{-31}$	$^3H_4 \rightarrow {}^3H_5$
Tm^{3+}	$1.3\cdot10^{-30}$	$0.2\cdot10^{-39}$	$^3H_6 \rightarrow {}^3H_4$

[a]The calculation was made for exciting radiation at a wavelength of 6328 Å.[15]

The relation between the transitions in electronic Raman scattering and the symmetry of the crystal field, which is shown for ions in solids, is also specified by Eqn. (14). The linear combination of the substates J_Z, which are the wave functions of the crystal field levels [Eqn. (10)], is in fact determined by the crystal field symmetry and the strength and symmetry of the field appear in the expressions for the mixing coefficients a.

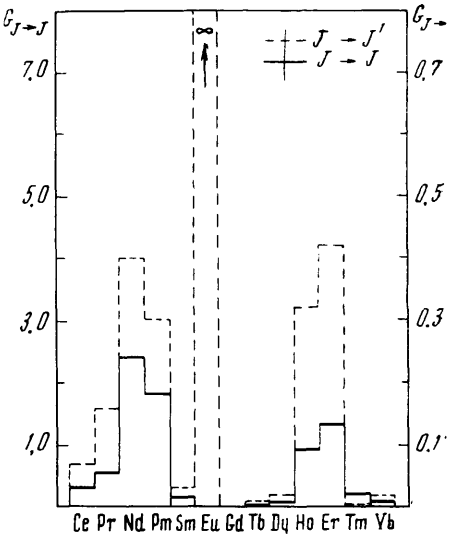


Figure 4. The calculated degree of antisymmetry of the tensor for electronic Raman scattering of tervalent lanthanide ions.

These coefficients and therefore the correct wave functions may be found by diagonalising the matrix comprising the elements $\langle J, J_Z | H_{CF} | J', J'_Z \rangle$, where H_{CF} denotes the effective potential due to neighbouring ions at the site of the jth electron of the lanthanide ion located in the centre. H_{CF} can be expressed in the following form:

$$H_{CF} = -e\sum_j V(r_j, Q_j, \varphi_j) \quad . \tag{17}$$

In the calculation of the crystal field, the perturbation Hamiltonian is usually formulated thus:

$$\mathcal{H}_{CF} = \sum_n \sum_{m=-n}^{n} \sum_j B_n^m r_j^m Y_j^m(\theta_j, \varphi_j) \quad . \tag{18}$$

The B_n^m are constants and their values are in principle determined by the positions and charges of the ions surrounding the lanthanide ions, r_j is the expectation radius of the jth $4f$ electron, and Y_n^m are spherical harmonics. The expansion for f electrons should include terms up to $n \leq 6$ subject to the condition $n \leq 2J$.

The eigenvectors, eigenvalues, the values of α_Q^K, and the elements of the tensor in terms of cartesian coordinates for the tervalent europium ion in a crystal field with tetragonal symmetry, determined by the parameters B_2^0, B_4^0, B_4^4, and B_6^0, are given in Table 3. Figs. 5, 6, and 7 illustrate the calculated polarised spectra of this ion in certain crystal fields.

The electronic transitions in Raman scattering are $^7F_0 \rightarrow {}^7F_1$ (<600 cm^{-1}) and $^7F_0 \rightarrow {}^7F_2$ (>600 cm^{-1}). All the

tensors for the transitions $J = 0 \rightarrow J = 1$ are fully antisymmetric and all the tensors for the transitions $J = 0 \rightarrow J = 2$ are fully symmetric. Such tensors may be separated from one another by the rotation of the entire crystal about the fourfold axis; the differences in Raman intensity under the conditions of the observation of $z(xy)x$ for the symmetrical tensor and the fully antisymmetric tensor are presented in Fig. 8. Table 3 shows that the coefficients a are completely independent of the crystal field parameters and consequently the number of Raman lines in the spectra obtained for different polarisations is the same for all the crystal fields with tetragonal symmetry, but the frequency of the Raman lines depends in all cases on the parameters B_n^m.

Table 3. The eigenvalues, eigenvectors, and scattering tensors for the Eu^{3+} ion in a tetragonal crystal field[a,b].

Eigenvalue	Eigenvector	Controlling element α_Q^K	$\alpha_Q^K/F(K,\nu)$	Scattering tensor
		$^7F_0 \rightarrow {}^7F_2$		
$2\alpha A_2 + \beta(A_4^0 - A_4^4)$	$(1/\sqrt{2})(\lvert 2,2\rangle - \lvert 2,-2\rangle)$	α_{-2}^2	$+(1/70)^{1/2}$	$\alpha_{-2}^2\begin{bmatrix} 1/2 & -i/2 & 0 \\ -i/2 & -1/2 & 0 \\ 0 & 0 & 0 \end{bmatrix}$
$2\alpha A_2^0 + \beta(A_4^0 + A_4^4)$	$1/\sqrt{2}(\lvert 2,2\rangle - \lvert 2,-2\rangle)$	α_2^2	$+(1/70)^{2/2}$	$\alpha_2^2\begin{bmatrix} +1/2 & -i/2 & 0 \\ -i/2 & -i/2 & 0 \\ 0 & 0 & 0 \end{bmatrix}$
$-\alpha A_2^0 + 4\beta A_4^0$	$1(\lvert 2,1\rangle \lvert)$	α_1^2	$-(1/35)^{1/2}$	$\begin{bmatrix} 0 & 0 & -1/2 \\ 0 & 0 & -i/2 \\ -1/2 & -i/2 & 0 \end{bmatrix}$
$-\alpha A_2^0 - 4\beta A_4^0$	$1(\lvert 2,-1\rangle \lvert)$	α_{-1}^2	$+(1/35)$	$\alpha_{-1}^2\begin{bmatrix} 0 & 0 & -1/2 \\ 0 & 0 & -i/2 \\ -1/2 & -i/2 & 0 \end{bmatrix}$
$-2\alpha A_2^0 + 6\beta A_4^0$	$1(2,0\rangle)$	α_0^2	$-(1/35)$	$\alpha_0^1\begin{bmatrix} -2/\sqrt{6} & 0 & 0 \\ 0 & -1/\sqrt{6} & 0 \\ 0 & 0 & 2/\sqrt{6} \end{bmatrix}$
		$^7F_0 \rightarrow {}^7F_1$		
$-2\alpha A_2^0$	$1(\lvert 1,0\rangle \lvert)$	α_0^1	$-(1/21)^{1/2}$	$\alpha_0^1\begin{bmatrix} 0 & i/\sqrt{2} & 0 \\ -i/\sqrt{2} & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$

[a] For $^7F_2$, $\alpha = -11/315$ and $\beta = 2/189$. For $^7F_1$, $\alpha_1 = -1/2$.

[b] All the A_n^m are expressed in cm^{-1}.

A complication is observed for lanthanide ions with an odd number of electrons. The assignment of the crystal field levels with respect to the symmetry of the scattering tensor elements and the wave functions is now based on irreducible representations for binary groups. All the crystal field levels are Kramers doublets and the double degeneracy may be removed when the ions are placed in a magnetic field. Table 4 gives the tensors and designations of the Raman lines shown for two Ce^{3+} transitions in $CeCl_3$—one from the $J_Z = \pm 5/2$ level to $J_Z' = \pm 3/2$ and another from the $J_Z = \pm 5/2$ level to $J_Z' = \pm 1/2$.

Thus, when a field is superimposed, it is possible to observe the individual components and the spectra for different polarisations may be constructed on the basis of the contributions of the scattering tensors to individual transitions. For one of the transitions in a zero field, the tensor is somewhat asymmetric. The frequency dependence of the degree of antisymmetry for the Ce^{3+} ion in $CeCl_3$ has been calculated[29]. It is illustrated in Fig. 9. The results depend greatly on the position of $\tilde{\nu}_{\chi k}$ which is ν_{4f5d} in our case. The presence of Kramers doublets in fact leads to a scattering tensor which differs from the normal tensors. Table 5 lists the characters of the binary group D_2 representations. All the crystal field states of the split LST manifold of a lanthanide ion with an odd number of f electrons belong to the representation Γ_5. Thus the transformation properties of the irreducible tensors $\Gamma_{\alpha_Q^K}$ are contained in the direct product of the representations $\Gamma_5 \times \Gamma_5 = \Gamma_1 + \Gamma_2 + \Gamma_3 + \Gamma_4$. The resultant overall tensor is therefore more complicated than the tensor for the vibrational transition of the system, which belongs to the usual point group D_2.

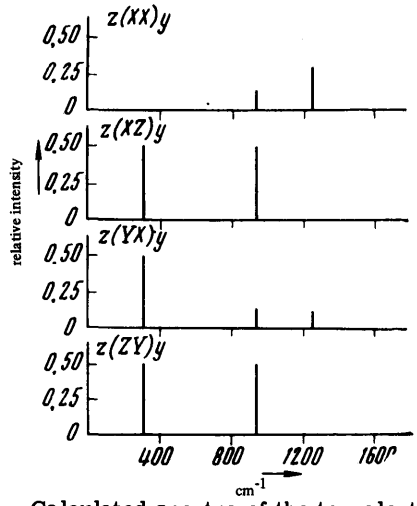


Figure 5. Calculated spectra of the tervalent europium ion in a crystal field of cubic symmetry for different polarisations. The intensities of the Raman lines with frequencies of about 800 cm^{-1} in Figs. 5 and 6 should be divided by 30 if the first excited electronic configuration has an energy of about 110000 cm^{-1}. The crystal field parameters are $A_4^0 = -250$ cm^{-1} and $A_4^4 = 5A_4^0$, where $A_n^m = \langle r^n \rangle B_F^m$.

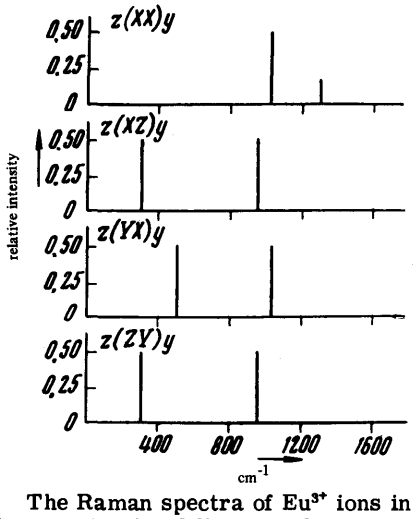


Figure 6. The Raman spectra of Eu^{3+} ions in a field with hexagonal symmetry for different polarisations. The crystal field parameters are $A_2^0 = 250$ cm^{-1} and $A_4^0 = -250$ cm^{-1}.

The calculation of the Raman spectrum for a specific polarisation presented here presupposes that the crystal unit cell contains one lanthanide ion and that the local axes of this ion are parallel to the macroscopic axes of the crystal. In most cases the situation is more complicated: the unit cell may contain more than one ion and the ions may occupy different sites with their own crystal field symmetry.

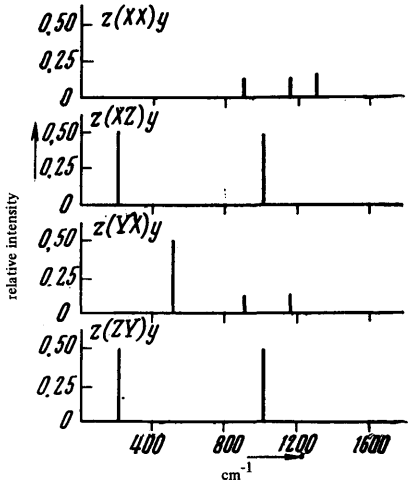


Figure 7. The Raman spectra of Eu^{3+} ions in a crystal field of tetragonal symmetry for different polarisations. The crystal field parameters are $A_2^0 = 250\ cm^{-1}$, $A_4^0 = -250\ cm^{-1}$, and $A_4^4 = -1000\ cm^{-1}$.

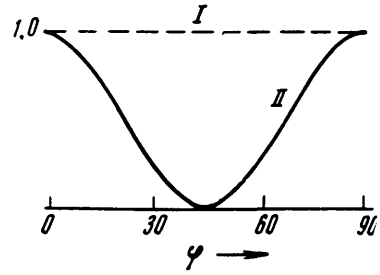


Figure 8. Variation of the Raman line intensity determined by the tensor element α_{yz} with the angle of rotation $\varphi°$ about the z axis of the crystal. Curves I and II refer to the asymmetric tensor $\begin{matrix}0\,a\,0\\-a\,0\,0\\0\,0\,0\end{matrix}$ and the symmetric tensor $\begin{matrix}0\,a\,0\\a\,0\,0\\0\,0\,0\end{matrix}$ respectively.

It is readily seen that the characteristics of the scattering by lanthanide ions are obtained for the entire crystal by the transformation of the scattering tensors $(\alpha_{\rho\sigma})^S_{kn}$ for each of the ions occupying different sites S in the laboratory coordinate system. This can be done with the aid of the rotation matrices R_S and R_S^{-1}, subsequent squaring of the individual tensor components, and their addition. The following scattering tensor is then obtained for the crystal:

$$[(\alpha_{\rho\sigma})_{kn}]^2_{\text{crystall}} = \sum_{\text{sites}} [R_s (\alpha_{\rho\sigma})^S_{kn} R_s^{-1}]^2.$$

Although this procedure is simple, it is clear that the interaction between various lanthanide ions is not taken into account. Indeed, it is possible to consider this case as one where there is incoherent scattering by the ions, in contrast to the case of coherent scattering. As has been shown by the present author and Schaack[12] it is then important to take into account the similarity between the factor-group interaction and the correlation between various phases of the scattering centres—lanthanide ions.

Table 4. The eigenvalues, eigenvectors, and Raman line intensities for the $^2F_{5/2}$ set of levels in a hexagonal crystal field.

$J_z - J'_z$ transition	Energy	Controlling element α_Q^K	$\alpha_Q^K/F(K,\nu)$	Intensity matrix
$-\frac{5}{2} \to -\frac{5}{2}$	$\frac{2}{3}\frac{4}{5}A_2^0 - \frac{3}{2}\frac{2}{1}A_4^0$	$\alpha_1^1 A_1^2$	$-\frac{2}{7}\sqrt{10/21}$ $\frac{6}{7}\sqrt{1/14}$	$\begin{bmatrix} 0 & \frac{1}{2}(a-b)^2 & \frac{1}{2}(a-b)^2 \\ \frac{1}{2}(a+b)^2 & 0 & 0 \\ \frac{1}{2}(a+b)^2 & 0 & 0 \end{bmatrix}$
$\frac{5}{2} \to \frac{3}{2}$	$\frac{2}{3}\frac{4}{5}A_2^0 - \frac{3}{2}\frac{2}{1}A_4^0$	$\alpha_{-1}^1 \alpha_{-1}^2$	$\frac{2}{7}\sqrt{10/21}$ $\frac{6}{7}\sqrt{1/14}$	
$-\frac{5}{2} \to -\frac{1}{2}$	$\frac{4}{3}\frac{6}{5}A_2^0 + \frac{3}{2}\frac{4}{1}A_4^0$	α_2^2	$\frac{3}{7}\sqrt{1/7}$	$\begin{bmatrix} \frac{1}{4}c^2 & \frac{1}{4}c^2 & 0 \\ \frac{1}{4}c^2 & \frac{1}{4}c^2 & 0 \\ 0 & 0 & 0 \end{bmatrix}$
$\frac{5}{2} \to +\frac{1}{2}$	$\frac{4}{3}\frac{6}{5}A_2^0 + \frac{2}{2}\frac{4}{1}A_4^0$	α_{-2}^2	$\frac{3}{7}\sqrt{1/7}$	

Table 5. The active representations for the D_2 binary group.

Representation	Components in cartesian coordinates	Irreducible components
Γ_1	$\alpha_{xx}, \alpha_{yy}, \alpha_{zz}$	α_2^2, α_0^0
Γ_2	$\alpha_{xy} \pm \alpha_{yx}$	$\alpha_2^2 - \alpha_{-2}^2, \alpha_0^1$
Γ_3	$\alpha_{xz} \pm \alpha_{zx}$	$\alpha_1^2 + \alpha_{-1}^2, \alpha_1^1$
Γ_4	$\alpha_{yz} \pm \alpha_{zy}$	$\alpha_{-1}^2 + \alpha_{-1}^2, \alpha_{-1}^1$
Γ_5	all the levels of the crystal field of the LSJ manifold	

Suppose that $\mathcal{H}_0$ is the Hamiltonian of an ion with a definite local symmetry, Φ_{ks} the wave function for the state k, and H_i the perturbation Hamiltonian describing the interionic energy. In the space group symmetry operations, H_i is transformed in the same way as H_0. The eigenfunctions Ψ_k for the $H_0 + H_i$ states with $k = 0$, which are important and of interest only in the case of first-order Raman scattering considered here, belong to an irreducible representation of the factor-group. In

terms of the zeroth approximation, these wave functions have the following form

$$\Psi_k = (1/N)\sum_s A_{ks}\Phi_{ks}.$$

With the exception of A_{ks}, these symbols have the usual significance. The A_{ks} are constants which have been chosen in such a way that the wave functions Ψ_k have been transformed in terms of the factor-group representations. Evidently the determination of A_{ks} is of primary importance.

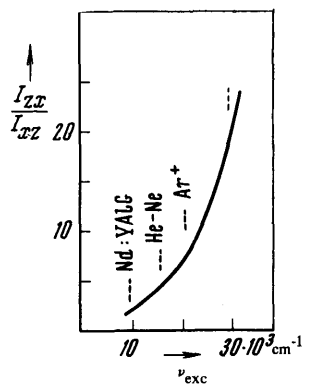


Figure 9. The ratio of the intensities I_{ZX} (related to the α_{ZX} element) and I_{XZ} (related to the α_{XZ} element) for Raman scattering in the electronic transitions of the Ce^{3+} ion in $CeCl_3$ for various frequencies of the exciting radiation.

For example, it follows from Table 6 that there is a unique relation between the representations of the local group D_2 and those of the factor-group O_h, since the representations of the group C_h appear once in each case. This makes it possible to set up the wave functions Ψ_k on the basis of symmetry considerations alone. If the irreducible representation γ is one-dimensional, then A_{ks} will be a character of γ referring to the symmetry elements which transform the site k into the site s. For two- or three-dimensional representations, it is necessary to employ the rules for finding the symmetry coordinates employed in molecular physics[17].

Table 6. Relation between the local irreducible representations and the representations of the factor-group for lanthanide ions in garnets.

D_2 representations	O_h^a representations	D_2 representations	O_h^a representations
A	$A_{1g}+E_g+T_{2g}$	B_2	$T_{2g}+T_{1g}$
B_1	E_g+T_{1g}	B_3	$T_{2g}+T_{1g}$

[a]Only the transformation properties of the Raman scattering tensor are quoted.

If the wave functions Ψ_k are used to calculate in the usual way (the integral $\langle\Psi_n|\alpha|\Psi_k\rangle \neq 0$) the scattering tensor components, the tensor for the crystal unit cell may be evaluated by the superposition of site tensors but now one must take into account the different phase factors. In this instance one must also consider the orientation of local axes, the following expression being obtained for the Raman intensity:

$$[(\alpha_{\rho\sigma})_{kn}]^2_{\text{crystal.}} = \Big[\sum_{\text{sites}} A^*_{ns}A_{ks}R_s \times (\alpha_{\rho\sigma})^s_{kn}R_s^{-1}\Big]^2.$$

The angles of rotation, which are important for the R_S and R_S^{-1} matrices for different sites of the unit cell, are obtained most simply when the directions of the local axes are known.

Calculation of the incoherent and coherent scattering tensors leads in general to the same results, but there is also a difference. In the first case one finds that the tensor for the Raman lines is determined by tensors associated with definite representations of the factor-group. It is then impossible to obtain information about the site tensors. On the other hand, in the case of coherent scattering, such information may be obtained and there is a relation between the crystal scattering matrix elements and the analogous values for the sites.

V. THE BREAKDOWN OF SELECTION RULES

In previous sections it was stated that the low electronic levels of the tervalent europium ion belong to the states ^7F_J, where $J = 0, 1, 2, \ldots, 6$. The $^7F_0$ state is the lowest and the $^7F_1$, $^7F_2$, and $^7F_3$ states are at about 300, 900, and 1800 cm^{-1} respectively.

The selection rules for electronic Raman scattering of lanthanide ions are as follows[4,5]: $\Delta S = 0$, $\Delta L \leqslant 2$, and $\Delta J \leqslant 2$; according to the $\Delta J \leqslant 2$ rule[4], the $^7F_0 - {}^7F_3$ transition is forbidden. However, this selection rule is valid only when J can still be regarded as a "good" quantum number, i.e. in those cases where the distances between the crystal field components are small compared with the distances between the energy levels for the state of the free ion. For strong crystal fields, "good" quantum numbers yield only the representations of the local symmetry group, so that different values of J may become mixed in a single eigenstate. However, the mixing of the J depends not only on the strength of the crystal field but also on its symmetry, since certain values of J cannot become mixed in the crystal if the crystal field symmetry is sufficiently high (for example states with $J = 0$ and $J = 3$ are not mixed for D_4 symmetry). Thus a good example of the breakdown of the $\Delta J \leqslant 2$ rule is provided by a crystal with a strong crystal field and a low local symmetry of the lanthanide ion. Among all the lanthanide ions, the free Eu^{3+} ion has the lowest levels; in this case mixing of the J can be achieved most readily. On the other hand, the aluminate crystal matrix gives rise to a strong crystal field with the point group having the C_S symmetry for the position of the lanthanide ion[6]. Table 7 shows that the states of the crystal fields with $J = 3$ belongs to the representations A' (Hougen and Singh[3]) and A'' (Elliott and Loudon[4]), but the wave functions of these states presumably contain an admixture of states with other values of J (particularly with $J = 2$). As a result, the Raman scattering in the $^7F_0$—$^7F_3$ electronic transition becomes allowed and the non-zero components of the scattering tensor again belong to the representations A' and A'' of the group C_S. It is possible to show in the same way that the Raman scattering in the $^7F_0$—$^7F_4$ transition is also allowed, but the intensity of these transitions

will presumably be much lower, because (1) the difference between the energies of the $^7F_2$ and $^7F_4$ levels is now about 2000 cm^{-1} and the states are mixed to a smaller extent than are the $^7F_3$ and $^7F_2$ levels where $\Delta E \simeq 800$ cm^{-1} and (2) the Raman intensity is proportional to the fourth power of the frequency of the emitted radiation.

Table 7. Symmetry properties of the crystal field levels for the ^7F_J set of $EuAlO_3$.

^7F Set	Representations of C_S groups	^7F Set	Representations of C_S groups
0	A'	2	$2A' + 3A''$
1	$A' + 2A''$	3	$3A' + 4A''$

α_{xx}, α_{yy}, α_{zz}, and α_{xy} enter into A'. α_{yz} and α_{xz} enter into A''.

The effect of the mixing of the J states has also certain interesting consequences for antisymmetric and isotropic tensors. Eu^{3+} ions provide a good example of the former. According to theory, the $^7F_0 - ^7F_2$ transitions are related to the more usual symmetric tensors. If the wave functions of the $^7F_1$ and $^7F_2$ states are mixed, then evidently the scattering tensors for the $^7F_0 - ^7F_1$ transitions now become partly antisymmetric and correspondingly some of the tensors for the $^7F_0 - ^7F_2$ transitions may change from symmetric to partly antisymmetric. The degree of antisymmetry depends on the percentage admixture of the corresponding states. The isotropic scattering tensor α_0^0 cannot contribute to transitions for the free ion either within the limits of a single configuration or to interconfigurational transitions. This follows from an examination of the conditions for a non-zero value of the $3j$-symbol introduced previously. However, as in the breakdown of the selection rule for the transitions with $\Delta J = 3$ and 4 in Raman scattering, the isotropic tensor can also contribute to the intensity under the influence of the mixing of the J states. From the theoretical standpoint, it is useful to recall that the absolute magnitude of $|\alpha_0^0|$ is about 100 times greater than $|\alpha_Q^{1,2}|$ and in the case of $^7F_0 - ^7F_2$ transitions it is easier to observe the presence of the isotropic tensor than that of the antisymmetric tensor.

In formulating the expressions for the scattering tensor, it was postulated that the frequency of the incident radiation (ν_0) is strongly displaced in relation to the frequency of the absorption band of the system. In this instance, when ν_0 is close to the value for the absorption band of the lanthanide ion, the Raman intensity for the transition between the ground stage g and the final state e is determined by the following scattering tensor:

$$(\alpha_{\rho\sigma})_{gl} = \sum_r \frac{\langle e|\rho|r\rangle\langle r|\sigma|g\rangle}{h\nu_0 - h\nu_{gr} + i\gamma_r} + \frac{[\rho \leftrightarrow \sigma]}{h\nu_0 + h\nu_{rl} + i\gamma_r} \quad . \qquad (19)$$

Here $\langle e|\rho|r\rangle$ and $\langle r|\sigma|g\rangle$ are the matrix elements of the operators ρ and σ of the electric dipole moment ($\rho, \sigma = x, y, z$; γ is the decay operator related to the line width of the electric dipole transition from the state g to the state r). In the derivation of Eqn. (19), we must assume that the matrix elements of the dipole operator become zero for transitions between states of the same parity. Thus only transitions between states with the $4f^n5s^25p^6$ configuration contribute, since owing to the crystal field states with configurations of other parities, similar to $4f^{n-1}5s^25p^65d$, become mixed in. If we designate by $|\alpha\rangle$ the lowest (as regards energy) configuration $|4f^n5s^25p^6\rangle$ and by $|\beta\rangle$ the first of the higher configurations $|4f^{n-1}5s^25p^65d\rangle$ of opposite parity, then one can write for the low states of the crystal field

$$|\Psi_1\rangle = a_1|\alpha\rangle + b_1|\beta\rangle + \ldots,$$
$$|\Psi_2\rangle = a_2|\alpha\rangle + b_2|\beta\rangle + \ldots,$$

where $\alpha_1 \simeq \alpha_2 \simeq 1$, $b_1 \simeq b_2 \simeq V_C/(E_\beta - E_\alpha)$, V_C determines the crystal field strength, and $E_\alpha - E_\beta$ determines the energy difference between the two configurations, equal to approximately 10^5 cm^{-1}. Here we are dealing with cases where V_C is between 10^2 and 10^3 cm^{-1} Then the values of b_1 and b_2 are also somewhere between 10^{-3} and 10^{-2}.[3]

An estimate of the matrix elements of the dipole moment operator is

$$\langle\Psi_1|\rho|\Psi_2\rangle \approx (a_1b_2 + b_1a_2)\langle\alpha|\rho|\beta\rangle \approx 10^{-2} \div 10^{-3}\langle\alpha|\rho|\beta\rangle.$$

Resonance implies that $\nu_0 \simeq \nu_{gr}$ and, if one assumes that the denominator of the first term in Eqn. (19) becomes equal to approximately ten, then this term has an order of magnitude somewhere between 10^{-5} and 10^{-7} in units of $|\langle\alpha|\rho|\beta\rangle|^2$. The second term in Eqn. (19) may be neglected.

If we consider the part of the sum for which the intermediate state $|r\rangle$ belongs to the configuration $4f^{n-1}5s^25p^65d$, then the denominator, which depends on the energy, will be 10^5 and we obtain 10^{-5} in units of $|\langle\alpha|\rho|\beta\rangle|^2$ for the contribution of this part of the sum. Hence we see that, although the matrix elements $\langle\Psi_1|\rho|\Psi_2\rangle$ are in fact very small, they can have an appreciable influence in the case of resonance. One can reach the following two conclusions.

1. The resonance effect depends on the admixture of states with a different parity from the states of the lowest conformation of the crystal field and consequently should be more intense for stronger crystal fields.

2. When the symmetry point group contains an inversion centre, there should be no resonance effect, since a crystal field of this type does not involve the mixing of configurations of different parities.

The matrix element $\langle\Psi_1|\rho|\Psi_2\rangle$ depends also on whether ρ is equal to x, y, or z. Thus the properties of the polarisation of the transition from the ground state to the resonance state have a direct influence on the Raman scattering tensor. In the special case where a direct transition between the two states is forbidden, we would not observe any resonance effect. However, the corresponding absorption line will of course also be missing under these conditions.

VI. EXPERIMENTAL METHODS

The apparatus for the investigation of Raman scattering is illustrated schematically in Fig. 10. It can be seen that the direction of propagation of the laser radiation is at right angles to the direction of the scattered light. In the general case the laser is focused in a very narrow beam within the crystal. Estimates of the beam diameter in our experiments yielded about 150—200 μm. The crystal was placed at the top of the cold finger of the experimental helium Dewar vessel fitted with windows for the illumination of the specimens and the observation of the scattered light. The light from the laser beam within the crystal was reflected onto the slit of a double monochromator.

Double monochromators are now used in Raman spectroscopy, since they are particularly effective in eliminating the scattered light and make it possible to observe Raman lines displaced by less than 10 cm^{-1} from the unperturbed Rayleigh line. In most cases a photomultiplier is used as a detector; in our experiments we employed a photomultiplier with an S20 cathode. The signal from the photomultiplier was transferred to an integrating digital voltmeter, the time constant of which was set in the range from 1 to 60 s. By reducing the scanning rate of the monochromator to 1.25 Å min^{-1}, it is possible to employ time constants of about 20 s. In order to prevent the distortion of the line form of the radiation, the slit width S, the time constant t, and the scanning rate v must be related as follows: $tv/S = 1/2$. The details of the detector are shown schematically in Fig. 10. A photomultiplier of type EMI 9558B was used in the experiments. The solenoid was placed directly around the photocathode; the light emerging from the output slit of the monochromator was focused by lenses onto a small section of the photocathode. The magnetic lines of force generated by the solenoid prevented the incidence on the first dynode of the photoelectrons emitted from different parts of the cathode, except its centre on which the scattered light impinged. This gave rise to an effective amplification of the signal to noise ratio by a factor of approximately six compared with the case where the magnetic field was switched off and the entire area of the photocathode was illuminated. The crystals employed in the experiments were very small and the length of the path traversed by the laser beam within the crystal hardly exceeded 4 mm in all cases. It is well known that the width of the electronic levels depends greatly on the temperature of the specimen. The lower the temperature, the smaller the width of the electronic level. For this reason, transitions between electronic levels were investigated at low temperatures.

However, such investigations suffer from the disadvantage that the principal characteristic of the Raman spectrum, the presence of anti-Stokes and Stokes lines, is lost if the specimen is cooled to very low temperatures. Nevertheless, for electronic levels in the region up to 150 cm^{-1} even at specimen temperatures below 77°K, there are excited lines with sufficient populations to ensure an adequate intensity of the anti-Stokes spectrum. In order to determine which line in the Raman spectrum of the crystal is due to Raman scattering in an electronic transition, the phonon spectrum of the lattice-matrix was compared, for example, with the spectrum of a lanthanide compound. The appearance in the latter of new lines might have been an indication that Raman scattering in electronic transitions takes place. However, the study of the phonon spectra of lanthanide compounds of the garnet type showed that marked differences are observed in the positions of the phonon bands for different lanthanide garnets. This implies that additional lines observed in the spectra of lanthanide compounds are not necessarily electronic Raman lines. A reliable method for determining which lines in the Raman spectrum belong to electronic transitions involves placing the specimen in strong magnetic fields. The low electronic levels of lanthanide ions in the crystal are sensitive to the influence of external magnetic fields; this is of course not the case for phonon lines. Fig. 10*c* presents details of the experimental apparatus in which the crystal is placed within a superconducting magnet fitted with the necessary apertures whereby it is possible to illuminate the crystal with laser light and to observe the scattered radiation at right angles to the direction of propagation of the laser beam. The specimen

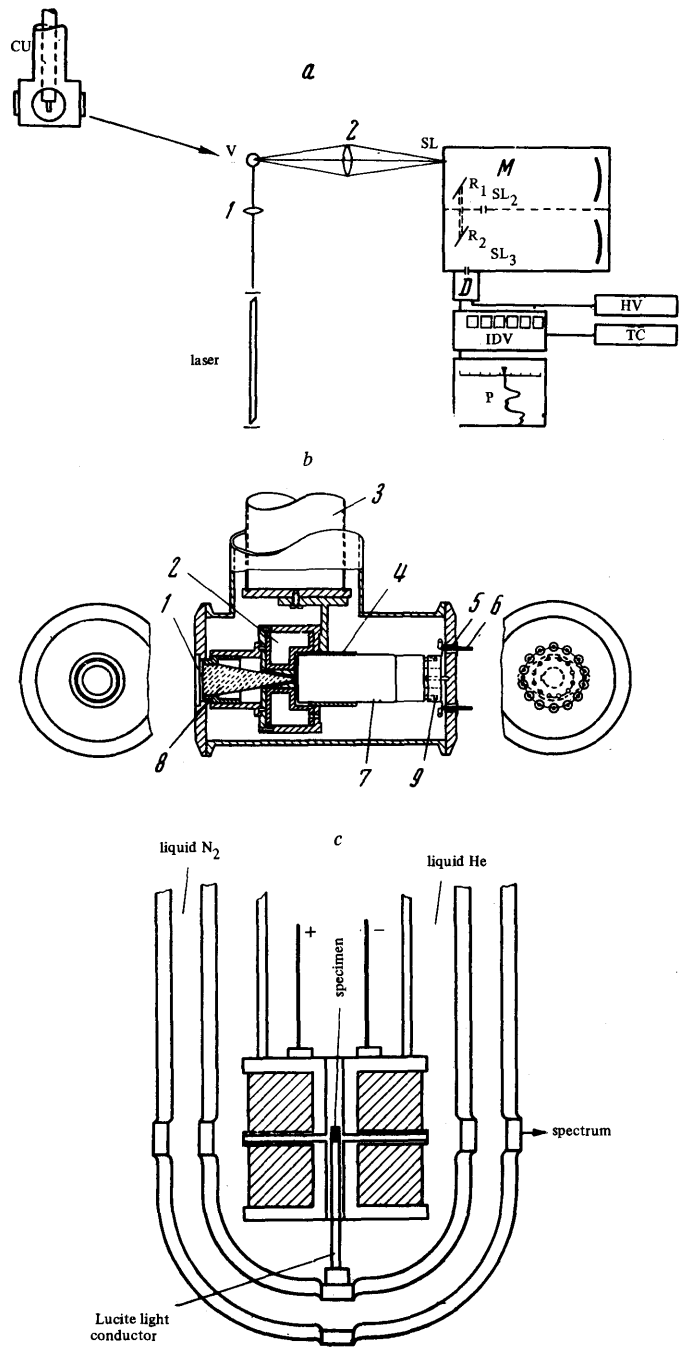


Figure 10. *a*) Diagram of apparatus for the measurement of Raman spectra with laser excitation: V—Dewar vessel containing the single crystal [the laser radiation is focused by the lens (*1*) into the interior of the crystal]; D—detector; HV—high voltage source; IDV—integrating digital voltmeter; P—pen recorder; TC—device for the measurement of the voltmeter time constant; M—double monochromator; CU—cuvette; SL—slit; R—replica gratings. *b*) Detector with cooling system and magnetic defocusing: *1*) Pyrex window; *2*) coil; *3*) to Dewar vessel; *4*) copper tube; *5*) glass—metal seal; *6*) photomultiplier terminals; *7*) photomultiplier; *8*) Pyrex light conductor. *c*) Schematic illustration of the position of the specimen in the superconducting magnet.

is now immersed in liquid helium and, needless to say, at this low temperature the anti-Stokes Raman lines should not be observed. An advantage of experiments at such temperatures is of course that the electronic levels under these conditions are very narrow. Care must be taken to screen the photomultiplier from the magnetic field generated by the superconducting magnet.

Having discussed the theory and the experimental conditions in the study of electronic Raman scattering, we now proceed to Section VII, which discusses the experimental aspects of electronic Raman spectroscopy.

VII. EXPERIMENTAL RESULTS‡

The Raman spectra of lanthanide ions in single crystals are discussed in this section. Consequently, apart from the excitation of the electronic levels, the phonons of the crystal–matrix will play a certain role. In the theoretical Section IV it was shown that the scattering cross-section for electronic transitions is lower than for vibrational Raman scattering and therefore it is more convenient to investigate lanthanide compounds which contain a high percentage of lanthanide ions. Such systems may be found in the series of rare-earth chlorides ($RECl_3$) [3,30] or their aluminates ($REAlO_3$). The phonons for the latter lattice-matrix are observed at frequencies <600 cm^{-1} and Fig. 11 illustrates part of the $SmAlO_3$ spectrum containing Raman lines in the range 1000–1550 cm^{-1}. According to the energy level diagram presented in Fig. 1, transitions of the type $^6H_{5/2} - {}^6H_{7/2}$ are to be expected in this region. The width of these transitions depends on the crystal temperature, which distinguishes between them and phonons and the data presented in Fig. 11 make it possible to establish immediately the position of the four crystal field components for $J = 7/2$. Raman scattering in electronic transitions within the limits of the $^6H_{5/2}$ configuration cannot be observed as they coincide in position with the intense phonons of the aluminate crystal. Another example of such systems has been found in the series of RE_2O_3 crystals[31]. The compounds Yb_2O_3 and Er_2O_3 were investigated and electronic transitions at a frequency of about 41 cm^{-1} were found for the erbium compound. The phonon level of the Yb_2O_3 and Er_2O_3 crystals differ also in their width which may indicate the occurrence of an electron–phonon interaction. The crystals of lanthanide oxides are cubic, another series of crystals of the same symmetry being provided by lanthanide garnets. Here we are interested in the lanthanide aluminium and gallium garnets with the general formulae $RE_3Al_5O_{12}$ or $RE_3Ga_5O_{12}$. The unit cell contains 80 atoms and the 237 degrees of freedom of the species may lead to a complex spectrum. By virtue of the cubic symmetry of the crystals, the appearance of only 21 vibrations active in Raman scattering is expected in the spectrum; the corresponding lines were observed in the spectra of many crystals containing aluminium and gallium in the range 40–900 cm^{-1}. Thus, as for the aluminates, here too it is convenient to investigate the electronic effects outside the phonon region.

Fig. 12 presents the spectra for different polarisations of the compound $Tb_3Al_5O_{12}$ with cubic symmetry. The spectrum arises as a result of transitions from the ground state (which is one of the levels of species $^7F_6$) to levels of species $^7F_5$. The local symmetry of the lanthanide ions in the garnet crystals is determined by the point group with D_2 symmetry since all the levels belong to one of the representations A, B_1, B_2, or B_3 of this group. For a transition of the type $A(^7F_6)$–$A(^7F_5)$, the tensor is determined by components transformed in accordance with the representations $A_{1g} + E_g + T_{2g}$; the tensor is the same also for transitions between levels with the symmetry $B_1(^7F_6)$ and $B_1(^7F_5)$, etc.§ However, since the symmetry of the crystal field is known, it is possible to predict how many times tensors of the type $A_{1g} + E_g + T_{2g}$, $E_g + T_{1g}$, and $T_{2g} + T_{1g}$ will appear. By altering the illumination conditions, it is possible to show that the symmetry of the ground state is A or B_1.

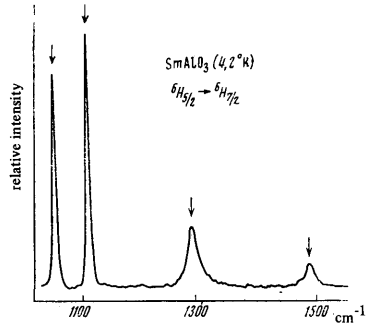


Figure 11. Low-temperature Raman spectrum of a non-oriented $SmAlO_3$ single crystal; the arrows indicate the $^6H_{5/2}$–$^6H_{7/2}$ electronic transitions.

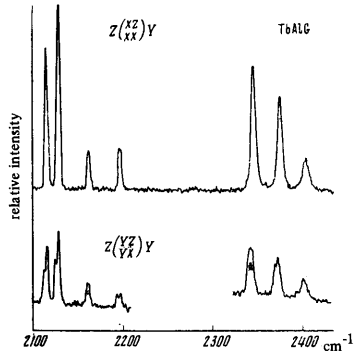


Figure 12. Raman spectrum of terbium aluminium garnet at 4.2°K. The lower spectrum is that of a crystal placed in a magnetic field of about 2.5 kG.

Having thus at one's disposal two possible sets for the assignment of states of the type $^7F_5$ in a crystal field with D_2 symmetry, it is now possible to employ the mathematical procedure used in crystal field calculations. In such calculations it was assumed that the ground state has the A symmetry and that the excited state with B_1 symmetry lies more than 10 cm^{-1} above the ground state.

‡The results presented in this section have been selected from data which have already been published[3,10,18,19,21,23].

§ See also Table 6.

It is most convenient to assign particular symmetries to the electronic levels using a spectroscopic technique based on electronic Raman scattering. The transitions in luminescence or absorption are usually largely related to the electric dipole moments and the moments in the directions x, y, and z for a cubic crystal cannot be distinguished. The dipole moment operator is transformed in accordance with one of the representations of the factor-group and therefore one cannot achieve a symmetry assignment for the crystal field levels. The electronic transitions for the $^7F_5$ levels in Raman scattering have frequencies below 600 cm^{-1} and this region also contains the phonons of the garnet crystal. Electronic Raman scattering can be separated from the phonon spectrum by comparing the spectrum in Fig. 13 with that of the yttrium–aluminium garnet. The positions of the corresponding phonons for the two crystals are established with the aid of identical polarisation measurements in Raman spectra. The high intensities of the electronic transitions in the range from 60 to 90 cm^{-1} are somewhat surprising. The general conclusion from data for TbAlG is that not all possible electronic transitions are observed. Evidently the width of the transitions continues to increase if the difference between the energies of the electronic levels reckoned from the lowest set of levels increases. Thus the width of the excited levels remote from the lowest level may be so great that it is difficult to observe the transitions, particularly if the phonons of the crystal-matrix are present.

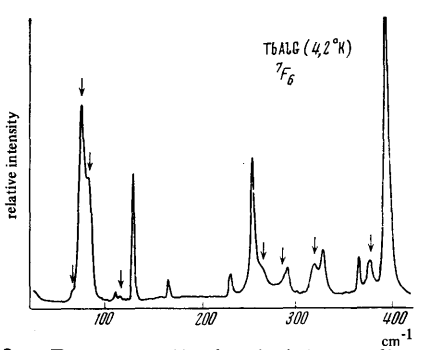


Figure 13. Raman scattering in interconfigurational electronic transitions of the type $^7F_6$ in TbAlG.

The foregoing considerations are confirmed by the data in Fig. 14. Like the main set of Tb^{3+} levels, Tm^{3+} ions also have the quantum number $J = 6$ in the ground state. Thus the crystal field with D_2 symmetry has 13 components but only two transitions have been observed for TmAlG. Under the same experimental conditions (power of the laser, quality of the crystal, recording system, etc.), it was found that the scattering at the electronic levels of the Tm^{3+} ion is definitely smaller than for the Tb^{3+} ion in the aluminium garnet crystal. This is at least consistent with the *ab initio* calculations of the absolute cross-sections presented in Table 2.

The changes in the spectra arising because the levels and the tensor components belong to representations of binary groups can be most satisfactorily demonstrated for $DyAl_5O_{12}$. The tensors for the phonons of this compound belong to the factor-group O_h. The space group of the garnet is O_h.[10] Fig. 15 illustrates part of the low-temperature Raman spectrum of DyAlG. Experiments showed that the upper spectrum is due to phonon (and electronic) levels with the E_g symmetry only. The lower Raman spectrum reflects only the transitions with T_{2g} symmetry. Evidently the phonons have the E_g or T_{2g} symmetry.

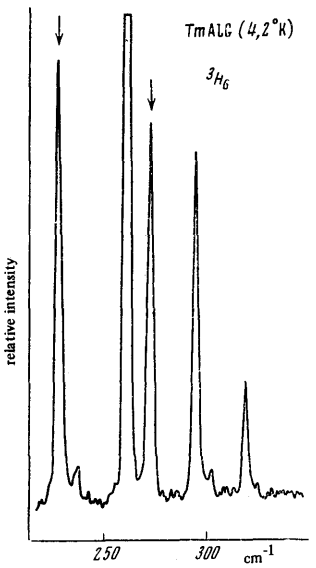


Figure 14. Raman scattering in two electronic transitions in thullium aluminium garnet.

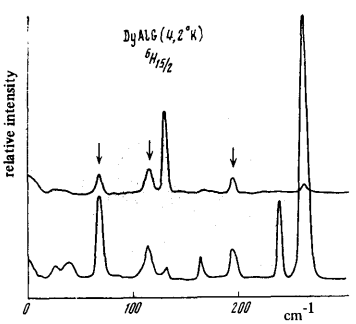


Figure 15. Polarisation Raman spectrum of an oriented crystal of dysprosium aluminium garnet. The difference between the polarisation characteristics of the electronic (↓) and phonon transitions becomes clear when the upper and lower spectrograms are compared.

The tensor for electronic transitions is contained in the representation $\Gamma_5 \times \Gamma_5 = \Gamma_1 + \Gamma_2 + \Gamma_3 + \Gamma_4$ of the binary group D_2 (see also Table 5). Thus we find that, as a result, the tensor for the transitions between electronic levels with Γ_5 symmetry no longer belongs either to the E_g representation or to the T_{2g} representation. This tensor is more complex and the spectra shown in Fig. 15

confirm the theoretical predictions. The Raman spectroscopic data for the electronic transitions in DyAlG have also been used to determine the crystal field strength expressed in terms of the coefficients A_n^m. The results of the calculation of the crystal field using data for electronic Raman scattering are important not only for the prediction on the basis of the crystal field parameters of the positions of the crystal field levels but also for the determination of the symmetry of the states. Thus there are more experimental data than the parameters to be determined and such data are now being used to find the parameters for all possible lanthanide garnets. Fig. 16 presents part of the Raman spectrum of $EuGa_5O_{12}$ (europium gallium garnet). According to theory, the observed electronic transitions of the type $^7F_0 - ^7F_1$ are due to a fully antisymmetric tensor. For cubic crystals, there are several methods for the determination of the tensor symmetry. It is impossible to distinguish symmetrical and antisymmetric tensors when the crystal is oriented in such a way that the excited radiation is propagated along the a axis of the garnet crystal and the scattered radiation is observed along the b and c axes. This situation differs radically from the case where the crystal is rotated by 45° about the c axis so that the direction of propagation of the incident radiation makes an angle of 45° with the a and b axes and the direction of observation of the scattered light is at right angles to them, as in all normal cases.

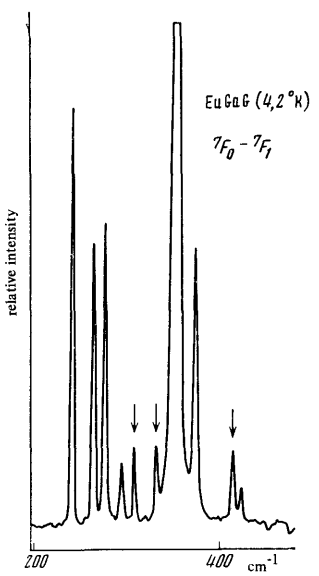


Figure 16. Electronic Raman scattering of Eu^{3+} in europium gallium garnet. The scattering corresponds to fully antisymmetric tensors.

Lanthanide ions occupy sites with D_2 symmetry and in the unit cell there are six such sites. Using the theory of the incoherent and coherent Raman scattering tensors, it is possible to set up the corresponding matrices taking into account the rotations; they are presented in Table 8.

Evidently, if the entire intensity is internally related to a phonon with E_g symmetry, then the intensity ratio $R = I_{yx+yz}/I_{zx+zz}$ becomes zero for the Raman line with A_g symmetry, 8/3 for the line with T_{1g} symmetry (antisymmetric tensors), and 4/3 for the line with T_{2g} symmetry (symmetrical tensors). The tensors which transform as the T_{1g} representation of the factor-group are of the form $(\alpha_{xy} - \alpha_{yx}, \alpha_{yz} - \alpha_{zy}, \alpha_{xz} - \alpha_{zx})$ and those which transform as the T_{2g} representation are $(\alpha_{xy} + \alpha_{yx}, \alpha_{yz} + \alpha_{zy}, \alpha_{xz} + \alpha_{zx})$.

Table 8. Scattering matrices for an oriented EuGaG crystal.

Tensor symmetry	Scattering matrix	Tensor symmetry	Scattering matrix
A_{1g}	$\begin{bmatrix} a^2 & & \\ & a^2 & \\ & & a^2 \end{bmatrix}$	T_{2g}	$\begin{bmatrix} c^2 & 0 & c^2 \\ 0 & c^2 & c^2 \\ c^2 & c^2 & 0 \end{bmatrix}$
E_g	$\begin{bmatrix} b^2 & 3b^2 & 0 \\ 3b^2 & b^2 & 0 \\ 0 & 0 & 4b^2 \end{bmatrix}$	T_{1g}	$\begin{bmatrix} 0 & d^2 & d^2 \\ d^2 & 0 & d^2 \\ d^2 & d^2 & 0 \end{bmatrix}$

It has been found experimentally that $R = 2.6 \pm 7\%$ for the 308 cm^{-1} line and $R = 2.6 \pm 10\%$ for the 329 cm^{-1} line. Owing to the presence of the phonon with T_{2g} symmetry close to the electronic transition at 411 cm^{-1}, it is impossible to determine the ratio R in this case. The experimental results show that two of the $^7F_0 - ^7F_1$ transitions indeed involve antisymmetric tensors. The first electronic Raman spectrum obtained on laser excitation was that of yttrium gallium garnet doped with europium[6] so that it is now evident that transitions due to the antisymmetric tensor were recorded as early as 1966.

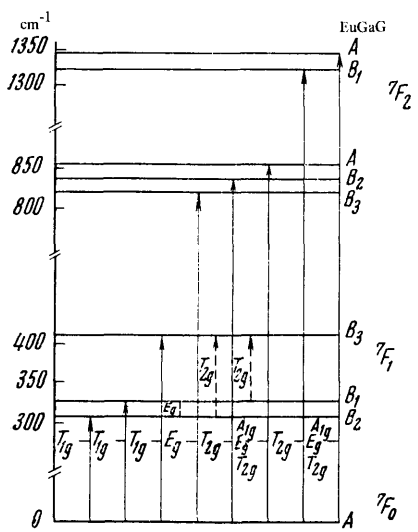


Figure 17. Low energy levels of Eu^{3+} in EuGaG.

Raman scattering has also been observed in electronic transitions of the type $^7F_0 - ^7F_2$; according to theory,

these transitions are linked to symmetrical tensors. The low energy levels of EuGaG obtained from Raman spectroscopic data are presented in Fig. 17. The presence of a level with B_1 symmetry in the gap between the levels with B_3 and B_2 symmetries for $^7F_1$ suggests that the crystal field is orthorhombic and the deviation from tetragonal symmetry is large. Thus, although the crystal is in fact cubic, the europium ion is in a crystal field determined by the local orthorhombic symmetry. Using in the analysis the mathematical procedures of the crystal field theory, it is possible to calculate the eigenvectors of the crystal field levels; the results of the calculation are presented in Table 9.

Table 9. Energies and assignments with respect to symmetry and the wave functions of the low-lying ^7F set of energy levels for EuGaG.

^7F_J State	Absorption of fluorescence	Frequency of Raman lines, cm^{-1}	Calc.[a]	Symmetry	Symmetry in terms of the basis function in $\|J_z\rangle$
$^7F_1$	305	308	308	B_2	$(1/\sqrt{2})(\|1_g1\rangle+\|1_g\bar{1}\rangle)$
	328	329	330	B_1	$\|1_g0\rangle$
	407	411	412	B_3	$(1/\sqrt{2})(\|1_g1\rangle-\|1_g\bar{1}\rangle)$
$^7F_2$		819	854	B_2	$(1/\sqrt{2})(\|2_g1\rangle-\|2_g\bar{1}\rangle)$
	833	834	869	B_3	$(1/\sqrt{2})(\|2_g1\rangle+\|2_g\bar{1}\rangle)$
	870	855	899	A	$\|20\rangle, (1/\sqrt{2})(\|2_g2\rangle+\|2_g\bar{2}\rangle)$
	1294[b]				
	1324	1324	1265	B_1	$(1/\sqrt{2})(\|2_g2\rangle-\|2_g\bar{2}\rangle)$
	1343	1341	1286	A	$\|20\rangle, (1/\sqrt{2})(\|2_g2\rangle+\|2_g\bar{2}\rangle)$
$^7F_3$	1830[b]	1832			
	1851[b]	1853			
	1894[b]	1896			
	1925[b]	1929			
	1977[b]	1982			
	2068[b]	1982			

[a] Calculation without taking into account the mixing of the J states for the following values of the parameters: $A_2^0 = -50$, $A_2^2 = 260$, $A_4^0 = -330$, $A_4^2 = 275$, $A_4^4 = 1400$.

[b] According to the data of Sonnich-Mortensen, and Koningstein[14].

Table 10. Fluorescence line frequencies at 77°K, Raman spectra, and frequency assignments for $EuAlO_3$.

Observed frequencies	Assignment	Energy of state, cm^{-1}	Raman line frequencies ($^7F_0 - ^7F_J$)
17 208	$^5D_0$—$^7F_0$	$^7F_0$: 0	
16 944		264	274
16 859	$^5D_0$—$^7F_1$	$^7F_1$: 350	356
16 735		474	476
16 266		942	945
16 240		968	968
16 195	$^5D_0$—$^7F_2$	$^7F_2$: 1013	1009
16 169		1039	1034
15 939		1269	—
15 388		1820	1814
15 382		1826	1824
15 354	$^5D_0$—$^7F_3$	$^7F_3$: 1854	1856
15 306		1902	1900
15 267		1941	1942
15 256		1952	1952

Calculation of all the Raman lines presupposes, as stated in the theoretical section, a complete analysis of the diagrams of energy levels belonging to set ^7F_j.

The selection rule $\Delta J \leq 2$ for electronic transitions does not hold either for EuGaG or $EuAlO_3$. The results of the study of the Raman and fluorescence spectra of $EuAlO_3$ are presented in Table 10 and Fig. 18 also shows the spectra and the energy level diagram.

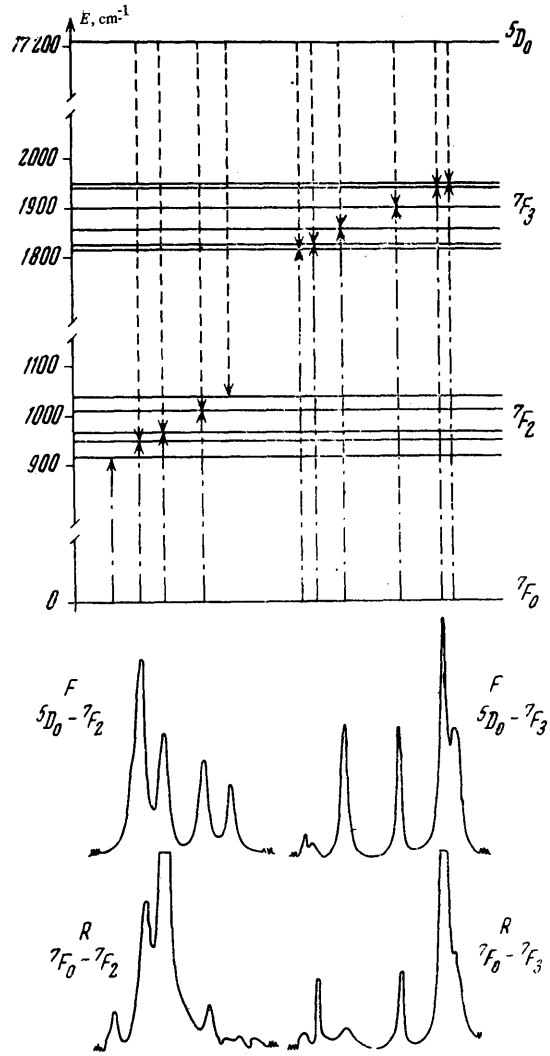


Figure 18. Transitions associated with the fluorescence and Raman scattering in europium aluminate.

The breakdown of the selection rule $\Delta J \leq 2$ occurs owing to the mixing of the J states, since the europium ion in the garnet and aluminate crystals is subjected to powerful crystal fields. The theory of the calculation of Raman intensities was applied to $CeCl_3$ and $PrCl_3$ crystals. A good agreement with experiment was found for $CeCl_3$. It was discovered that one of the Raman lines is linked with a partly asymmetric tensor. The calculated degree of asymmetry agrees satisfactorily with experimental data, possibly owing to the simplicity of the energy level scheme for Ce^{3+}. There is a good agreement between theory and experiment also for $PrCl_3$. The calculations are simple,

since the crystal field is determined by a small number of parameters.

We shall now turn our attention to the results of studies on resonance Raman scattering and the Zeeman effect in Raman scattering. The observation of electronic Raman scattering involved serious experimental difficulties. Firstly, it was necessary to find a system where at least one of the electronic absorption bands coincides with the available laser lines. The majority of absorption spectra of crystals with lanthanide ions contain a large number of lines in the green and blue regions of the visible spectrum and therefore there is some probability of a coincidence with the emission lines of the argon laser. Indeed a fairly large number of such cases have been found but only some of them are suitable for the investigation of resonance Raman scattering.

It was discovered that under these conditions not only the frequencies but also the oscillator strength of the chosen transition must satisfy special requirements. If the oscillator strength is too low, there is no interaction and consequently there is only a slight increase of the Raman intensity, while in the opposite case the entire exciting laser light is absorbed in a thin layer on the surface of the crystal. Although the resonance effect can in fact occur under these circumstances, the Raman scattering is too weak to be detected. Thus the optimal conditions should be sought when (a) the laser line coincides with an absorption band of moderate intensity and (b) when the specimen does not absorb in the part of the spectrum containing the Raman lines.

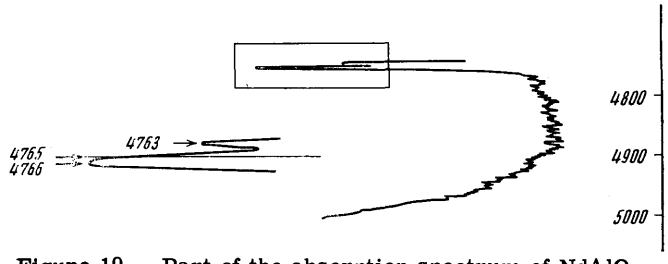


Figure 19. Part of the absorption spectrum of $NdAlO_3$ in the region of the 4765 Å line of the argon laser.

In our particular case the most serious difficulty involved making sure that the observed lines are indeed due to electronic Raman scattering and not to fluorescence. Fig. 19 presents the absorption spectrum of Nd^{3+} in $NdAlO_3$, which is involved in resonance with the 4765 Å line of the argon laser. Fortunately there is no complete coincidence in this case. The laser line is located at the wing of the absorption line on the high-energy side and it is displaced by approximately 4 cm^{-1} relative to its centre. If the observed emission lines (Fig. 20) were due to transitions caused by fluorescence from this level to lower levels, there would have been a 4 cm^{-1} shift relative to the Raman spectrum. Such a shift is not observed. The positions of the two low levels were known from the Raman spectrum obtained on excitation by the 4880 Å laser line; they were established for the first time by Scott[5]. Fig. 19 shows that there is a window in the absorption spectrum of the crystal between 4770 and 4950 Å. The intensity of the Raman lines in this region does not change owing to partial absorption. The Raman lines excited by those of the argon laser at wavelengths of 4765 and 4880 Å, which occur in this region, can therefore be compared directly with one another.

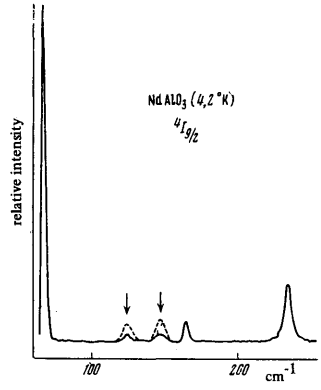


Figure 20. Raman spectrum of $NdAlO_3$ excited by light corresponding to the line at wavelengths of 4765 Å (shown dashed) and 4880 Å.

The spectra obtained with and without resonance, i.e. excited by laser lines at wavelengths of 4765 and 4880 Å, are compared in Fig. 20. The 53 and 147 cm^{-1} lines are due to phonons, while the 125 and 146 cm^{-1} lines are associated with electronic Raman scattering at the electronic levels. The phonon lines can be used as a standard in adjusting the spectra illustrated in Fig. 20 to the same intensity scale. Indeed the Raman spectrum excited by the 4765 Å line has a lower intensity owing to the partial absorption of the laser emission. Fig. 20 shows that the intensity of the electronic line increases approximately by a factor of five in the case of resonance. This small increase of intensity is inconsistant with the considerations put forward in Section V. It is found that not all the components of the scattering tensor increase in resonance Raman scattering. The symmetry of the resonating excited levels plays a role here, but, owing to the low symmetry of the $NdAlO_3$ crystal and because of the complexity of the tensor for scattering in electronic transitions (binary groups!), no attempts were made to determine the components of this tensor. Resonance scattering has also been observed for the Nd^{3+} ion in yttrium gallium garnet and for the Dy^{3+} ion in garnet crystals. All the data indicate that the dipole transitions within the limits of the $(4f)^n$ configuration have a weak influence on the elements of the scattering tensor for electronic transitions compared with the contributions having a direct bearing on the matrix elements. The case where the exciting line is in resonance with an interconfigurational transition has been observed for the Ce^{3+} ion in CaF_2; the enhancement of the electronic transitions was more marked, since the oscillator strength for the absorption band was much greater than for the $4f-4f$ transitions forbidden according to the Laporte rule.

The first studies on the Zeeman effect in Raman scattering were reported for the tervalent ytterbium ion in

yttrium gallium garnet. Here we shall consider the influence of this effect on the positions of the very intense electronic transitions of ytterbium aluminium garnet centred at 80 cm^{-1} (Fig. 13). The Zeeman spectrum of this Raman line is illustrated in Fig. 21, which shows that, for a zero magnetic field, cooling of the specimen from 77°K to 4.2°K alters the shape of the line. The intensity of the B transition at a frequency of 81.5 cm^{-1} decreases on the side of high energies. Since it has a higher energy than the A transition with a frequency of 74.6 cm^{-1}, one may reach certain conclusions concerning the energy level scheme; the relative positions of the levels are illustrated in Fig. 21. When a magnetic field is imposed, the distance between the two lower levels of the $^7F_6$ set of the TbAlG crystal field increases. The temperature of the crystal was 4.2°K, being immersed in liquid helium and the first excited state was unpopulated. Accordingly, the transition between levels with A (in group D_2) and B_3 or $B_2(D_2)$ symmetry disappears if the field and the distance between the levels increase. The single transition from the ground state shifts from 74.6 cm^{-1} to 79.5 cm^{-1} in a field of about 48 kG. In the crystal lattice unit cell of the garnet there are six sites for lanthanide ions, but the above experiments failed to reveal a fine structure. To some extent, this has also been observed for Dy^{3+} in garnets and one can now assume that the Zeeman Raman spectroscopic technique may be important, particularly in those cases where it is necessary to distinguish phonons and electronic transitions.

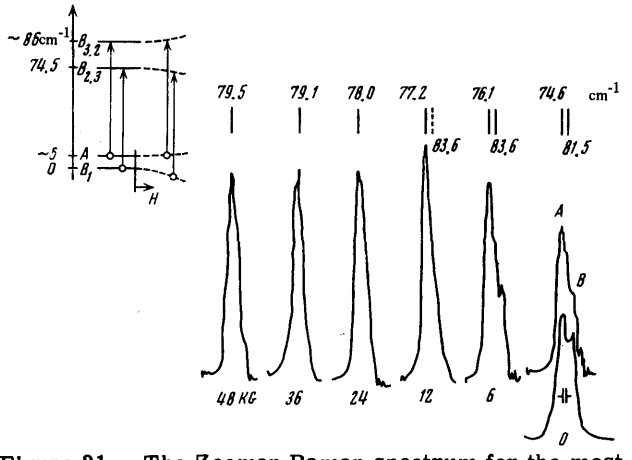


Figure 21. The Zeeman Raman spectrum for the most intense electronic effects in terbium aluminium garnet.

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The present review deals exclusively with the interpretation and observation of light scattering at low electronic levels of lanthanide ions in solids. This type of light scattering is weaker than the usual scattering at vibrational levels but it has certain theoretical (and experimental) features which are not encountered in the usual Raman spectroscopy. All the experimental results presented are to some extent related to the effect of the crystal field on the lanthanide ion. It has been established that these results are particularly important for the elucidation of the nature of the crystal field in certain cubic crystals. Investigations of this kind have now been extended, particularly to the crystal field of transition metal ions in solids. Only limited information is available on this subject, but it appears that the main interest lies in the magnetic properties of transition metal compounds reflected in the characteristics of the scattering spectra.

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Faculty of Chemistry,
Carleton University,
Ottawa, Canada

U.D.C. 543.878;547.52/59

The Reactivities of .OH, $.O^-$, and HO_2. Radicals and Oxygen Atoms in Aqueous Solutions of Aromatic Compounds

N.A.Vysotskaya

This review considers the results of studies on the reactivities of hydroxy- and perhydroxy-radicals and oxygen atoms with respect to aromatic derivatives of benzene, pyridine, and furan. The rate constants for the reactions investigated have been compared and a relation between them and the structure of compounds oxidised has been demonstrated.
The bibliography includes 60 references.

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I. INTRODUCTION

The ·OH, $\cdot O^-$ and $HO_2\cdot$ radicals and atomic oxygen are formed in many oxidation-reduction processes used in the manufacture of important organic products, biochemical oxidation, and purification of sewage. Owing to their high reactivity, these radicals react rapidly with substances in solution and with one another and therefore their concentration in solutions is very low, which makes it difficult to investigate reactions involving them. Competitive methods, which make it possible to determine by comparatively simple procedures the relative rate constants for these reactions, and also pulse radiolytic methods, whereby the absolute rates may be determined, have been extensively applied to the study of processes of this kind.

The review presents the data obtained in recent years on the kinetics of reactions of ·OH and $\cdot O^-$ radicals with aromatic compounds; this makes it possible to revise many generally accepted hypotheses concerning the mechanisms of these reactions and the properties of the radicals themselves. The results of kinetic studies on the reactions of $HO_2\cdot$ radicals and atomic oxygen in the $O(^3P)$ state, which are as yet very few, have been examined.

II. REACTIONS OF ·OH RADICALS

Catalytic and photochemical decomposition of hydrogen peroxide or the radiolysis of water are used to generate ·OH radicals in aqueous solutions.

It was established in recent years that the active oxidising species formed in the decomposition of H_2O_2 by the above procedures and in the radiolysis of water are identical. This conclusion is based on a comparison of the relative rates of oxidation of the same substrates (benzene and many of its derivatives, methyl and ethyl alcohols, and certain other compounds) in the radiolysis of water and in the catalytic or photochemical decomposition of hydrogen peroxide in the presence of the same ·OH radical traps. *NN*-Dimethyl-*p*-nitrosoaniline (DMNA),[1,2] thymine[3], or H_2O_2 (Armstrong[4]) were used as the ·OH radical traps. The absolute rate constants listed in Table 1 were calculated from the ratios found.

Table 1 shows that the rate constants for the oxidation of substrates by products of the photochemical and catalytic decomposition of hydrogen peroxide are very close to the values obtained for the radiation-induced oxidation. This is consistent with the formation of free hydroxy-radicals in the photochemical and catalytic decomposition of hydrogen peroxide, since the generation of ·OH radicals in the radiolysis of water is not in doubt[6]. In $H_2O_2 + M^{+n}$ systems in the absence of organic additives, the hydroxy-radicals formed are captured by metal ions or their complexes with H_2O_2, which leads to the appearance of new paramagnetic complexes as shown by ESR spectroscopic data[7-10]. The results presented extend the scope of studies on the reactions of ·OH radicals.

Table 1. Comparison of the rate constants for the oxidation of various substrates by products of the photochemical or catalytic decomposition of H_2O_2 and the radiolysis of water.

Substrate	$10^{-9}k$, litre mole^{-1} s^{-1}			
	$H_2O_2 + h\nu$	$H_2O_2 + Fe^{2+}$	$H_2O_2 + Ti^{3+}$	$H_2O \xrightarrow{\gamma^{60}Co}$
Benzene	4.2[5]	4.1[5]	—	4.3[3], 3.8[1]
Benzyl alcohol	2.8[5]	—	—	4.1[1]
Benzoate ion	3.8[5]	—	—	4.1[1]
Anisole	5.0[5]	—	—	4.9[1]
Phenol	8.3[5]			7.5[1]
Methanol	—	0.8[5]; 0.89[4]	0.77[4]	0.75[3] 0.69[4]
Ethanol	—	1.1[5]; 1.7[4]	1.5[4]	1.6[3]
Formic acid	—	0.12[4]	0.12[4]	0.14[4]
Oxalic acid	—	0.016[4]	0.015[4]	0.02[4]

A number of studies were made recently on the interaction of these radicals with various organic acceptors[1-3,11-14]. The kinetics of these reactions with benzene and pyridine derivatives were investigated in detail by Shevchuk et al.[1] and with benzene also by Neta and coworkers[14,15]. Shevchuk et al.[1] and Neta and coworkers[14] employed the method of competitive kinetics using DMNA as the hydroxy-radical acceptor[2]. The systems

were irradiated with cobalt-60 γ-rays. The concentrations of DMNA before and after irradiation were determined spectrophotometrically.

For the competing reactions,

$$\text{Ac} + {}^{\cdot}\text{OH} \xrightarrow{k_1} \text{product},$$

$$\text{RH} + {}^{\cdot}\text{OH} \xrightarrow{k_2} \text{product},$$

it was shown that

$$\frac{1}{G_{(-\text{Ac})}} = \frac{1}{G_{\text{OH}}}\left[1 + \frac{k_2[\text{RH}]}{k_1[\text{Ac}]}\right].$$

where Ac = DMNA, RH = hydrocarbon and $G_{(\text{Ac})}$ and $G_{(\text{OH})}$ are the radiation-chemical yields for the disappearance of the acceptor and the formation of the ·OH radicals respectively.

This equation makes it possible to find the ratio k_2/k_1. Table 2 lists the relative rate constants for substituted benzenes and pyridines obtained by Shevchuk et al.[1] using this method. The logarithms of the $k_{\text{RH}}/k_{\text{benzene}}$ ratios are correlated with Hammett's σ constants. Shevchuk et al.[1] found a satisfactory correlation for substituted benzenes with $\rho = -0.31$. A similar value $\rho = -0.41$ was found by Neta and coworkers[14] using the same acceptor. Dorfman and Neta[15] determined the absolute rate constants for the hydroxylation of substituted benzenes by pulse radiolysis, from the formation curves for hydroxycyclohexadienyl radicals. The correlation between the logarithms of $k_{\text{RH}}/k_{\text{benzene}}$ and Hammett's σ constants yielded $\rho = -0.5$, which is fairly close to the values of ρ obtained by the method of competitive kinetics.

Table 2. Relative rate constants for the reactions of substituted benzenes, furans, and pyridines with hydroxy-radicals.

Substrate		$k_{\text{substrate}}/k_{\text{acceptor}}$
Substituted benzenes		
NHC_6H_5		1.04±0.04
OH (O^-)		0.68±0.02
OCH_3		0.45±0.04
I		0.40±0.02
CH_2OH		0.37±0.02
COO^-		0.37±0.01
Cl		0.36±0.05
H		0.35±0.01
CHO		0.35±0.03
NO_2		0.25±0.01
Substitute pyridines		
COO^-	α	0.13±0.01
Cl	α	0.14±0.01
H	α	0.16±0.01
Br	α	0.19±0.01
CH_3	α	0.20±0.01
O^-	α	0.38±0.01
NH_2	α	0.67±0.12
CN	β	0.06±0.01
$CONH_2$	β	0.08±0.01
Br	β	0.09±0.01
COO^-	β	0.18±0.02
CH_3	β	0.19±0.01
O^-	β	0.43±0.02
$CONH_2$	γ	0.12±0.01
COO^-	γ	0.21±0.01
O^-	γ	0.23±0.01
Cl	γ	0.25±0.01
NH_2	γ	0.40±0.01
2,6-CH_3		0.24±0.01
2,4-CH_3		0.25±0.01
α-Substituted furans		
CH_2OH		1.19±0.10
H		1.16±0.05
COO^-		0.92±0.16
CHO		0.62±0.04

Mention must be made of the discrepancies between the absolute rate constants obtained by pulse radiolysis and the values calculated from the relative constants obtained by the method of competitive kinetics. The former are as a rule higher by a factor of 2–3. The reason for the discrepancy is so far obscure. It may be related to the use of defective techniques in the first or second case[16] and possibly in both. However, comparison of the coefficients for the linear correlations of the rate constants obtained by different methods for series of identical derivatives shows a fairly satisfactory agreement between them.

The negative sign of ρ shows that the hydroxylation reactions are electrophilic; this is in turn consistent with data on the relative amounts of isomers formed[17] and demonstrates the electrophilic properties of the ·OH radicals. The low value of ρ, lower than in the usual electrophilic substitution reaction, suggests a high reactivity of the hydroxy-radicals as a result of which they are less sensitive to the polar influences of the substituents. Table 2 shows that the rate constants for the reactions of substituted pyridines are several times smaller than for benzene, in agreement with the lower reactivity of the pyridine ring in relation to attack by the electrophilic hydroxy-radicals. Accordingly, the absolute value of ρ is higher than for the series of benzenes and reaches 0.73. However, these reactions are also accelerated by electron-donating substituents and are retarded by electron-accepting substituents. A satisfactory correlation has been found only for β-substituted pyridines ($\rho = -0.73$).

The results obtained for the effect of substituents in the α-position are probably distorted by the adjacent electronegative nitrogen atom. The rate constants for the reactions of pyridine derivatives with electron-donating substituents in the α-position are higher than for the γ-substituted pyridines (Table 2). For compounds with electron-accepting substituents, the opposite relation between the rate constants for the oxidation of α- and γ-derivatives is observed. This may be because, as shown by Cercek and Ebert[18], hydroxy-radicals add not only to the ring but also partly to the pyridine nitrogen atom. In this process, the inductive effect of α-substituents at the nitrogen atom leads to the observed behaviour of the overall reaction rate constants and is of primary importance.

In contrast to the pyridine ring, furan derivatives readily undergo electrophilic substitution reactions and do not exhibit a tendency towards reactions with nucleophilic species. The relative rate constants for the reactions of furan and some of its derivatives[19] have been obtained by a method of competitive kinetics analogous to that employed by Shevchuk et al.[1] using the DMNA acceptor and were found to be higher by a factor of 2–3 than the corresponding constants for benzene derivatives and be a factor of 7 than for substituted pyridines (Table 2). This demonstrates an enhanced sensitivity of furan derivatives to attack by ·OH radicals. A satisfactory correlation has been found between $k_{\text{RH}}/k_{\text{furan}}$ and Hammett's σ constants with $\rho = -0.81$. The absolute value of ρ is relatively small and does not exceed those encountered in homolytic reactions ($1.5 > \rho > 0$). However, it is higher than the values found for reactions of substituted benzenes and pyridines, which may indicate a greater ease of transmission of the electronic effects of substituents in the furan series[20].

The high reactivity of hydroxy-radicals is consistent with the low activation energies for their reactions. The relative rate constants for reactions of ·OH radicals with various organic substrates have been determined[21] in the temperature range 20–70°C. Thymine was employed as the hydroxy-radical acceptor[3]. The observed activation

energies for reactions involving the abstraction of a hydrogen atom by hydroxy-radicals did not exceed 5 kcal mole^{-1} and those for addition reactions did not exceed 2 kcal mole^{-1}. The variations in activation energy in the benzene series relative to DMNA have been determined[19]. They are of the order of 0.08—0.56 kcal mole^{-1} and do not exceed the experimental error. The activation energies for β-substituted pyridines were found to be about ten times larger: 1.7 ± 0.2 kcal mole^{-1} for pyridine, 1.6 ± 0.3 kcal mole^{-1} for β-nicotinic acid, 2.1 ± 0.3 kcal mole^{-1} for β-nicotinamide, and 1.2 ± 0.1 kcal mole^{-1} for β-hydroxypyridine. It is evident from the above results that the activation energies for pyridine derivatives increase with the electron-accepting properties of the substituents and decrease as their electron-donating properties become more pronounced.

The data for the reactions of ·OH radicals with *ortho*-, *meta*-, and *para*-substituted phenols[22] are presented in Table 3. In order to determine the relative rate constants the DMNA acceptor was employed at pH 9 and isopropyl alcohol at higher pH values[23]. The logarithms of the relative rate constants for *para*-substituted phenols at pH 9 are satisfactorily correlated with Hammett's σ constants ($\rho = -0.32$). This value of ρ hardly differs from that obtained for the oxidation of benzene derivatives, which indicates a similarity of the mechanisms of these reactions. The correlation between the rate constants for *meta*-substituted phenols yielded $\rho = -0.18$. For *ortho*-substituted derivatives, there was virtually no correlation at pH 9 but it was observed at pH 13 with $\rho = -0.61$. This finding may be attributed to the influence of the dissociation of phenols at pH 13 on the *ortho*-effect.

Comparison of the relative rate constants for the reactions of substituted phenols with the analogous constants for the corresponding benzene derivatives shows that the former are higher by a factor of 2—3 (see the data in Tables 2 and 3). This is consistent with the powerful activating effect of the hydroxy-group in reactions with ·OH radicals.

Table 3. Relative rate constants for the reactions of substituted phenols with ·OH radicals at pH 9.

	Substituent	$k_{substrate}/k_{acceptor}$
para	$C(CH_3)_3$	1.49±0.26
	OCH_3	1.15±0.23
	CH_3	1.04±0.09
	CHO	0.82±0.2
	COO^-	0.70±0.06
	H	0.68±0.02
	NO_2	0.61±0.08
	OH	0.44±0.12
meta	OH	0.97±0.12
	Cl	0.58±0.05
	NO_2	0.57±0.05
ortho	CH_3	0.90±0.15
	OH	0.89±0.14
	NO_2	0.74±0.06
	CHO	0.69±0.16
	COO^-	0.69±0.09
	Cl	0.66±0.12

The introduction of a second hydroxy-group into the benzene ring activates the latter still further for reaction with ·OH radicals, but the introduction of a third ·OH group deactivates it, as can be seen from a comparison of the following absolute rate constants ($10^{-9}k$, litre mole^{-1} s^{-1}): 3.8 for benzene[1], 7.5 for phenol[1], 10.7 for 1,3-dihydroxybenzene, and 5.7 for 1,3,5-trihydroxybenzene[22].

This effect may be attributed to a change in the hydroxylation mechanism, for example, the site of attack by ·OH radicals changing from the benzene ring to the hydrogen atom of the phenolic hydroxyl.

The relative rate constants (with DMNA as the acceptor) for the reactions of ·OH radicals with carbohydrates, polysaccharides, and certain aromatic compounds have been determined[24,25]. The authors believe that the protective properties of radioprotectors (inositol, propyl gallate, trihydroxypyridine derivatives) can be accounted for by the high rate of their interaction with ·OH radicals.

III. REACTIONS OF ·O$^-$ RADICAL-IONS

The ·OH radicals are known to dissociate at high pH according to the mechanism

$$\dot{O}H + OH^- \underset{k_2}{\overset{k_1}{\rightleftarrows}} \dot{O}^- + H_2O \ ;$$

the pK_a for the dissociation is 11.8 ± 0.2 (Rabani and Matheson)[11] and the rate of the forward reaction is a thousand times higher than that of the reverse reaction[26]:

$$k_1 = (1.2 \pm 0.3) \cdot 10^{10}\ M^{-1}\ s^{-1},$$
$$k_2 = (9.2 \pm 0.2) \cdot 10^{7}\ s^{-1},$$

The study of the kinetics of the hydroxylation of organic substances in alkaline media at increasing pH values yielded information about the relative reactivity of the ·OH radical and its conjugate base ·O$^-$. It was found for reactions with phenols[22] that the relative rates of hydroxylation decrease with increase of pH (Tables 4 and 5). The following changes in the relative rate constants for the reactions of ·OH radicals with phenols have been found: 0.68 ± 0.02 at pH 9, 0.46 ± 0.10 at pH 12, and 0.28 ± 0.04 at pH 13. The constants at pH 13 are more than a factor of 2 lower than those at pH 9 (Table 4).

Table 4. Comparison of the relative rate constants for *ortho*-substituted phenols at pH 9 and 13.

Substituent	$k_{phenol}/k_{acceptor}$(pH 9)	$k_{phenol}/k_{acceptor}$(pH 13)
$-COO^-$	0.69±0.09	0.32±0.05
—CHO	0.69±0.16	0.27±0.06
$-CH_3$	0.90±0.15	0.33±0.03
$-OCH_3$	1.18±0.15	0.46±0.09

This is not related to the dissociation of the *ortho*-substituted phenols themselves, since, firstly, the formation of phenoxide ions would accelerate the addition of ·OH radicals because phenoxide anions are more powerful electron donors than the undissociated phenols and, secondly, at pH 12 and 13 phenols are completely ionised, while the ·OH radical is hardly dissociated at pH 9, at pH 12 the degree of dissociation is 50%, and at pH 13 the dissociation is almost complete. Consequently the decrease of the rate constants can be accounted for only by a lower reactivity of the radical-ions ·O$^-$ radicals compared with ·OH radicals. The data obtained for phenols agree with the conclusion[23] (Table 5) that ·O$^-$ is

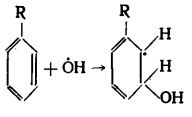
much less reactive in both addition and electron transfer reactions, while reactions involving the abstraction of a hydrogen atom take place with equal efficiency when either of the two species is involved.

Table 5. Comparison of the relative rate constants for the reaction of ·OH radicals in acid, neutral, and alkaline media[23].

Substrate	0.05 *M* H_2SO_4	pH 6.98	0.1 *M* NaOH	1.0 *M* NaOH	Substrate	0.05 *M* H_2SO_4	pH 6.98	0.1 *M* NaOH	1.0 *M* NaOH
$(CH_3)_2CHOH$	1.00	1.00	1.00	1.00	$(C_2H_5)_2O$	1.15	1.20	0.79	—
CH_3OH	0.29	0.36	0.39	0.47	I^-	6.9	8.0	1.82	1.70
CH_3CH_2OH	0.63	0.61	0.64	0.70	Br^-	1.97	1.95	0.03	—
$HCOO^-$	—	1.34	0.60	0.68	C_6H_6	2.2	2.3	0.05	—
HCOOH	0.06	—	—	—	C_6H_5OH	4.4	5.2	0.75	—

IV. THE MECHANISM OF HYDROXYLATION BY ·OH RADICALS

One may regard it as established that in the first stage hydroxy-radicals add to aromatic rings with the intermediate formation of hydroxycyclohexadienyl radicals[27-33] according to the mechanism



and do not abstract hydrogen from then with formation of phenyl radicals as suggested previously[34-38]. This is supported by the results of studies on the radiolysis of solutions of benzene in heavy water (D_2O) [29,30] and also by the direct observation of the spectra of hydroxycyclohexadienyl radicals in studies by pulse radiolysis[33] or by ESR in flow systems[32]. Hydroxy-radicals can also add initially to the substituent with a subsequent rearrangement involving a shift to the ring. It has been shown by pulse radiolysis[39] that ·OH radicals react with *p*-nitrophenol, adding to the nitro-group via the mechanism

$$\dot{O}H + OHC_6H_4NO_2 \rightarrow OHC_6H_4N\dot{O}_2 + H^+$$

with $k = (3.8 \pm 0.6) \times 10^9$ litre mole^{-1} s^{-1} and subsequent isomerisation of the resulting radical-ion into a hydroxycyclohexadienyl radical via the reaction

$$OH—C_6H_4N\dot{O}_2 + H^+ \rightarrow OH(OH)\dot{C}_6H_4NO_2 \quad ,$$

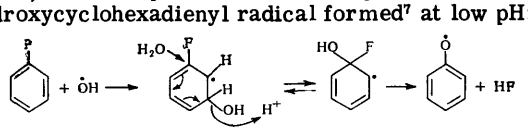
the pK_a of which is 14 ± 2 s^{-1}.

Hydroxy-radicals can also displace a ring substituent. For example, in the reaction between ·OH radicals and anisole, the methoxy-group is substituted with retention in the resulting phenol of the oxygen from anisole[40], in agreement with the following mechanism[41]:

$$C_6H_5OCH_3 + \dot{O}H \rightarrow C_6H_5\dot{O}CH_2 + H_2O \quad ,$$

$$C_6H_5\dot{O}CH_2 \xrightarrow{\dot{O}H} C_6H_5OCH_2OH \rightarrow C_6H_5OH + HCHO \quad .$$

However, such substitution also can occur with incorporation in the resulting phenolic hydroxyl of oxygen from water, for example via the acid fragmentation of the hydroxycyclohexadienyl radical formed[7] at low pH:



with subsequent conversion of the resulting phenoxy-radical into phenol containing oxygen from water.

A similar reaction can probably occur with benzene and many of its derivatives. For some of these, the incorporation of oxygen from water into the product of their oxidation by Fenton's reagent has been established[40,42]. The transfer of oxygen from water is not associated with a rapid exchange of hydroxy-radicals with water, as frequently suggested in the literature[43-45]. Indeed, calculation of the upper limit of the rate of exchange of hydroxy-radicals with water showed that it is slower by 3—4 powers of ten than the rate of reaction of these radicals with organic substances[46]: $0 \leq k < 7 \times 10^6$ litre mole^{-1} s^{-1}.

V. REACTIONS OF HO_2· RADICALS

The participation of HO_2· radicals in the hydroxylation of an aromatic ring has been postulated in a number of studies[47,48]. It has also been suggested that they do not possess electrophilic properties[47] and therefore yield different proportions of the isomeric products in the hydroxylation of the aromatic ring as compared with ·OH radicals and are less reactive than ·OH radicals towards aromatic compounds[49]. The reactivity of HO_2· radicals in aqueous solutions of aromatic compounds has been little investigated quantitatively. This is due to the difficulty of determining the rate constants for their reactions in the presence of the more reactive hydroxy-radicals, the mode of reaction of which is similar. There are only data for the oxidation of the sulphonates of indigo and certain other dyes, which have been obtained by the method of competing acceptors[50,51]. The relative rate constants for reactions of the dyes with HO_2· radicals generated by the γ-radiolysis of water were determined in such studies.

These reactions were carried out in the presence of oxygen in order to convert all the reducing species into HO_2· radicals; the pH was kept at 0.4 to avoid the dissociation of the HO_2· radicals (pK = 4):

$$H\dot{O}_2 \rightleftarrows H^+ + \dot{O}_2^-$$

and the reaction was carried out in the presence of added 2,5-dichlorohydroquinone which trapped quantitatively the ·OH radicals.

The rate constant for the reaction of HO_2· with the dye was calculated by considering the competition between the reactions

$$D + H\dot{O}_2 \xrightarrow{k_1} \text{colourless product} \quad ,$$

$$H\dot{O}_2 + H\dot{O}_2 \xrightarrow{k_2} H_2O_2 + O_2 \quad ,$$

where D is the dye, using the equation

$$k_1 = \frac{0.693}{D^0_{1/2}} \sqrt{\frac{2k_2 I}{\alpha G_{HO_2}}} \quad ,$$

where $k_2 = 2.2 \times 10^6$ litre mole^{-1} s^{-1},[52] I the dose rate, $G_{HO_2} = 3.6$ the radiation yield in the formation of HO_2· radicals,[53] $\alpha = 1.66 \times 10^{-23}$ mole ml mol.$^{-1}$ litre^{-1} a conversion factor, and $D^0_{1/2}$ the dose at which the concentration of the dye diminished by 50%.

Table 6 lists the rate constants obtained in this way. They are approximately a million times smaller than the rate constants for the reactions of ·OH radicals with aromatic compounds, which indicates a much lower reactivity of HO_2· radicals compared with hydroxy-radicals.

VI. REACTIONS OF ATOMIC OXYGEN

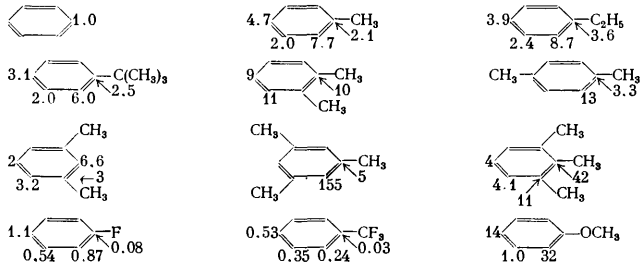
The hypothesis of the intermediate formation and involvement of atomic oxygen in the ground $O(^3P)$ state in chemical and radiation-chemical processes in aqueous solutions has already been put forward in the literature[47,54]. Certain studies have also been made on the reactivity of $O(^1D)$ atoms in solutions. These atoms were generated by the photolysis of ozone at 2537 Å.[55,56] However, since the reaction of $O(^1D)$ with water is very rapid, high concentrations of the corresponding traps are required.

Table 6. Rate constants for the reactions of $HO_2^{\cdot}$ radicals with indigo sulphonates.

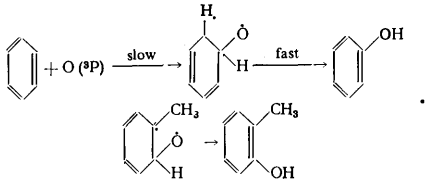
Dye	k_1, litre mole^{-1} s^{-1}
Indigo tetrasulphonate	$7.7 \cdot 10^2$
Indigo trisulphonate	$4.5 \cdot 10^3$
Indigo disulphonate	$8.5 \cdot 10^3$

The reactions of $O(^3P)$ oxygen in the ground state with aqueous solutions of aromatic compounds have been studied by the method of competing acceptors[57] developed by Amichai and Treinin[58]. $O(^3P)$ atoms were generated by the flash photolysis of BrO_3^- ions in the presence of molecular oxygen playing the role of the trap for $O(^3P)$. The partial rate factors for the formation of phenols in the reactions of $O(^3P)$ with substituted benzene were determined in the same study. The results are presented in Table 7.

Table 7. Partial rate factors for the formation of phenols in reactions of substituted benzenes with $O(^3P)$ at 30°C.



These data show that $O(^3P)$ atomic oxygen is electrophilic. The *ortho*-position is more reactive than the *para*-position, which is characteristic of radical reactions, for example those of ·OH radicals. A satisfactory correlation has been obtained ($r = 0.95$) with the logarithms of the partial rate factors for the *meta*- and *para*-positions and Hammett's σ^+ constant for $\rho = -1.15$. The negative sign of ρ indicates the electrophilic nature of $O(^3P)$, while the fairly high absolute value of ρ compared with the corresponding value for ·OH radicals is evidence of a greater selectivity of atomic oxygen compared with hydroxy-radicals. The following mechanism, analogous to that for hydroxylation by ·OH radicals, has been proposed for hydroxylation by atomic oxygen:



The low isotope effect found in the oxidation of an equimolar mixture of benzene and deuteriobenzene ($k_H/k_D = 1.14 \pm 0.04$) shows that the C—H bond is not dissociated in the rate-determining step of the reaction, in agreement with the proposed mechanism.

The absolute rate constant for the oxidation of benzene by atomic oxygen, determined by Grovenstein et al.[57], is $k_{25°} = 1.2 \times 10^7$ litre mole^{-1} s^{-1}.

Comparison of the reactivities of the radicals ·OH, $\cdot O^-$, and $HO_2^{\cdot}$ and the $O(^3P)$ oxygen atoms has shown that the hydroxy-radicals are the most reactive among them (Table 8). The reactivity of their dissociated form $\cdot O^-$ is somewhat lower (by a factor of 3—4). The oxygen atoms are less reactive than ·OH radicals approximately by a factor of 300 and the reactivity of the $HO_2^{\cdot}$ radicals is lower still—by 5—6 powers of ten.

In conclusion, we may mention that the rate constants for the reactions of hydroxy-radicals with organic compounds in aqueous solutions have been compiled by Metelitsa[48], Denisov[59], and Anbar and Neta[60].

Table 8. Comparison of the rate constants for the reactions of ·OH, $\cdot O^-$ and $HO_2^{\cdot}$ radicals and $O(^3P)$ oxygen atoms.

Species	k, litre mole^{-1} s^{-1} Compound oxidised		
	benzene	phenol	indigo disulphate
·OH	$3.8 \cdot 10^9$ [1]	$7.5 \cdot 10^9$ [1]	—
$\cdot O^-$	—	$2.1 \cdot 10^9$ [22]	—
$O(^3P)$	$1.2 \cdot 10^7$ [57]	—	—
$HO_2^{\cdot}$	—	—	$8.5 \cdot 10^3$ [61]

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Pisarzhevskii Institute of
Physical Chemistry,
Academy of Sciences of
Ukrainian SSR, Kiev

U.D.C. 547.922

New Aspects of Polycyclisation

E.S.Krongauz

The review deals with a comparative discussion of polycyclisation processes and the prospects of the polycyclisation method in the synthesis of thermostable polymers. The bibiography includes 221 references.

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I. INTRODUCTION

During the last 10–15 years, increasing attention has been devoted in many world scientific centres to an active search for new ways of synthesising polymers containing various cyclic groups in the macromolecules. The reason for this is, on the one hand, the ease of their formation due to the favourable thermodynamics and kinetics of such reactions (particularly of the formation of five- and six-membered systems) and, on the other hand, the importance and wide variety of their applications in man's practical activities.

The rapid development of these investigations is largely related to the fact that they are directed to the solution of one of the most urgent problems in the modern chemistry of macromolecular compounds presented by modern engineering techniques now being developed, namely the creation of materials with special properties.

The development of new macromolecule formation reactions led to the appearance of the class of polyheteroarylenes—polymers the macrochains of which consist of aromatic carbocycles and heterocycles. Many of these polymers have a high heat resistance and thermal and chemical stability, useful deformation-strength characteristics, satisfactory electrical conductivity and photoconductivity, etc.

A significant role of the same reactions in natural processes can be postulated with a high degree of probability, since, for example, cyclic forms are known to be important in the structure of protein. The pathways leading to the formation and decomposition of macromolecular compounds in nature are still obscure. However, the synthesis of high polymers which are the most important biologically—proteins, higher carbohydrates, and nucleic acids—and the study of their nature, metabolism, etc. are virtually impossible without simulating the functions of these natural compounds by synthetic polymers.

Studies in the field of cyclic polymers have been very numerous; the reactions used for their synthesis have also been extremely varied. Nevertheless, despite the different nature of these reactions, they can be combined under the single concept of polycyclisation, because they lead to polymeric structures the final form of which is in fact determined by cyclisation processes. The synthesis of a cyclic polymer can occur in a single-stage or via the formation in the first stage of an intermediate linear macromolecule containing fragments capable of subsequent cyclisation.

Processes already familiar, such as cyclopolymerisation and cyclocopolymerisation, the Diels–Alder reaction, 1,3-dipolar cycloaddition, polycyclotrimerisation, and polyheterocyclisation, are also polycyclisation reactions. The reactions enumerated above can be divided into two groups: (1) processes in which chain propagation is coupled to the formation of rings, as, for example, in Butler cyclopolymerisation and in polycycloaddition reactions and (2) single- or two-stage polyheterocyclisation processes (including the synthesis of ladder and parquet structures) and polycyclotrimerisation in which the stages involving the formation of linear and cyclic polymers may be separated.

The formation of polycyclic compounds constitutes an irreversible process and may be regarded as an example of non-equilibrium polymerisation reactions. The energy relations of these reactions and also their feasibility are mainly determined by the structural changes in the chemical bonds and by the appearance of qualitatively new bond systems.

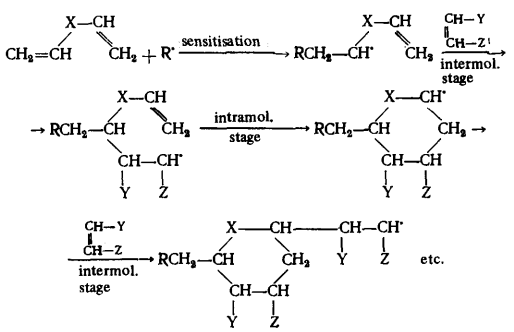
In the course of studies on these reactions, there has been a significant change in traditional ideas about functionality, introduced into polymer chemistry by its founder (Staudinger [1]), according to which it was believed that linear macromolecules can be formed only by the interaction of bifunctional polymers, while monomers with a large number of functional groups give rise to the formation of branched and cross-linked products. Polycyclisation is virtually based on tetrafunctional starting materials and leads ultimately to cyclolinear polymers.

In recent years investigators have paid increasing attention to the mechanism and kinetics of the formation of cyclochain polymers and also to a more detailed study of the properties of the latter. The results of the investigation of cyclochain polymers are described in an extensive original literature, in many review articles [2-14], and monographs [15-20].

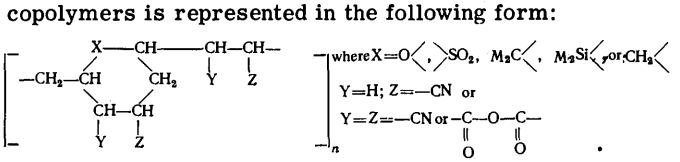
This review deals with a comparative discussion of polycyclisation processes and their influence on the properties of polymers, attention being concentrated on methods whereby thermostable polymers may be synthesised.

II. CYCLOPOLYMERISATION AND CYCLOPOLYMERISATION

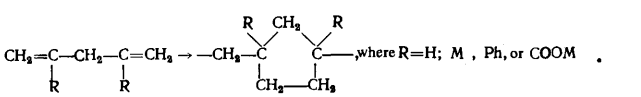
In 1951 Butler and Ingley [21] established that, contrary to theoretical predictions [1], dialkyldiallylammonium salts form non-cross-linked linear polymers and, in order to account for these results, put forward an intramolecular–intermolecular mechanism, which proved to be common to reactions involving the conversion of 1,6-dienes into cyclopolymers [22,23]. Later Butler [24,25] reported the copolymerisation of certain dienes with mono-olefins proceeding via an alternative intramolecular–intermolecular mechanism:



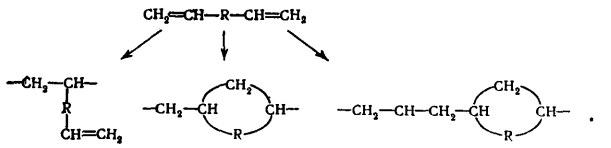
The first example of this kind was the cyclopolymerisation of vinyl ether and maleic anhydride; subsequently the reaction was extended to a wide range of dienes, alkynes and SO_2. [26-29] The general structure of the resulting copolymers is represented in the following form:



Apart from the fundamental work of Butler and coworkers, mention should be made of the wide range of studies by Marvel's school and many other investigators in which the scope of cyclopolymerisation was greatly extended and its kinetics and mechanism were investigated. Thus it was shown that symmetrical 1,5-dienes are polymerised similarly to 1,6-dienes with a high degree of cyclisation, forming polymers containing five-membered rings in the macromolecules [30-32]:

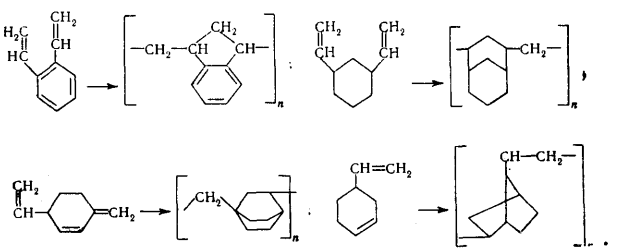


Asymmetric 1,5- and 1,6-dienes and other non-conjugated dienes are capable of homopolymerisation and cyclisation, particularly in those cases where the reactivities of the two double bonds are comparable; otherwise cyclopolymerisation, branching, and cross-linking reactions compete and the contribution of each to the overall process may vary considerably [33-35].



It was noted that the polymerisation of asymmetric dienes and the copolymerisation of two monomers have many features in common and the relation between the cyclisation and copolymerisation parameters is determined by the nature of the multiple bonds of the monomers [35]. Polymers containing different macrorings in the chain were obtained by the cyclopolymerisation of higher $\alpha\omega$-diolefins in which the double bonds are separated by 4–18 methylene groups [36-40].

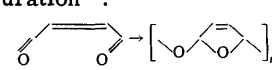
The polymerisation of dienes containing cyclic groups, which leads to the formation of bicyclic structures in the absence of steric hindrance, has been described. Thus *o*-divinylbenzene [41], *cis*-1,3-divinylcyclohexane and *cis*-1,3-divinylcyclopentane [42], and 1-methylene-4-vinylcyclohexene and 4-vinylcyclohexene [43] polymerise according to the following equations:



The formation of bicyclic and tricyclic structures is also possible in polymerisation of branched open-chain trienes and tetraenes; thus Trifan and coworkers [44] reported the synthesis of soluble polymers with a low degree of unsaturation from triallylethyl- and tetraallyl-ammonium bromides and also from 3-vinylhexa-1,5-diene.

The polymerisation of monomers containing double bonds between carbon atoms and heteroatoms, for example, dialdehydes [45-50], di-isocyanates [7,51], dinitriles [7,52], and epoxy-compounds, has been investigated in recent years.

Systematic studies on the effect of temperature, solvents, catalysts, and monomer concentration on the rate of polymerisation and on the molecular weight of the polymer formed have shown that the mode of reaction, its rate, and the polymer structure are determined not only by the nature of the monomer, but also to a considerable degree by the type of catalyst employed, its amount, the presence of water, and other factors [7]. Thus the studies of the structure of the polymer obtained by the cyclopolymerisation of maleic aldehyde by infrared and NMR spectroscopy have shown that, in contrast to cationic and Ziegler catalysts, anionic catalysts promote the formation of the *cis*-configuration [45]:

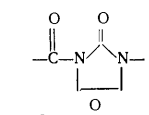
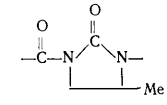
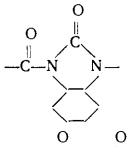
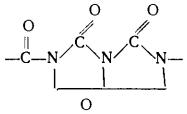
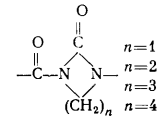


In the case of *o*-phthalodialdehyde, the amount of the *cis*-form is also determined by the catalyst employed,

decreasing in the following sequence: γ-irradiation > cationic catalysts ≥ anionic catalysts > coordination catalysts [50].

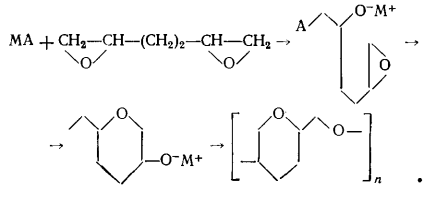
Anionic catalysts, polar solvent, and a temperature in the range between −50° and −75°C are most suitable for the cyclopolymerisation of di-isocyanates [7]. Polymers of this type are listed in Table 1.

Table 1. Cyclopolymers of aliphatic di-isocyanates [7].

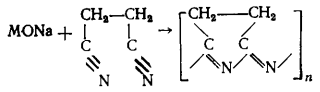
Monomer [a]	Structure of polymer unit	M.p., °C	β_{int} [b]	Solvent
1,2-Diethylene di-isocyanate [c]		365	0.85	H_2SO_4, TCE–phenol (40:60)
1,2-Triethylene di-isocyanate		287	1.35 0.56 [c] 0.72 [d]	HCOOH, DMSO, DMF, nitromethane
1,2-Cyclohexylene di-isocyanate		303	0.38	Pyridine, nitromethane, DMSO
1,2,3-Triethylene tri-isocyanate		365—400	0.28 [e]	H_2SO_4
αω-Polymethylene di-isocyanate		350 270—280 350 350		DMSO DMSO *m*-Cresol Ethylene carbonate

[a] Polymerisation in DMF between −30° and −50°C with NaCN as catalyst.
[b] β_{int} of 0.5% solution in 40:60 TCE–phenol mixture at 30°C.
[c] Polymerisation without catalyst.
[d] The molecular weight, determined osmometrically in nitromethane solution, is 45 000.
[e] Polymerisation in bulk at 0°C in a stream of nitrogen.
[f] In sulphuric acid.

The cyclopolymerisation of diepoxy-compounds can be achieved in the presence of a wide range of catalysts, which may include tri-isobutyl and tri-isopropyl-aluminium, PF_5–H_2O, diethylzinc, and others. Depending on the structure of the initial monomer, tetrahydrofuran or pyran rings are formed. The polymer having the highest molecular weight (η = 0.45 dl g^{-1}) but with limited solubility is that of 1,2,5,6-diepoxyhexane obtained in the presence of the $ZnEt_2$–H_2O system; the author suggested an anionic polymerisation mechanism [52]:



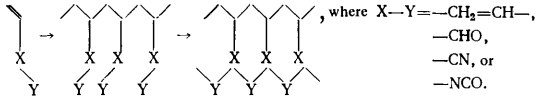
The cyclopolymerisation of various dinitriles in methanol in the presence of sodium methoxide via the mechanism



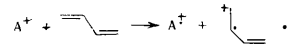
has been described [52]. n may vary, depending on the reaction conditions, from 6 to 65. There is a possibility of the incorporation in the polymeric skeleton of other structures, including the triazine structure.

Interesting results have been obtained in the study of the cyclopolymerisation of three types of bifunctional monomers with fixed (in the 2-position of the six-membered ring) double bonds [54]: (a) monomers with two C=C bonds (*o*-divinylbenzene, *cis*-1,2-divinylcyclohexane); (b) monomers containing two C=O bonds (*o*-phthalodialdehyde, *o*-formylphenylacetaldehyde); (c) monomers containing one C=O bond and one C=C bond (*o*-vinylbenzaldehyde). Although the structural characteristics of the monomers favour cyclopolymerisation, chain propagation in these polymers is different and is determined in the present case by the nature of the monomer. A stepwise chain propagation has been suggested for the cationic polymerisation of *o*-divinylbenzene; the polymerisation of monomers such as *cis*-1,2-divinylcyclohexane and *o*-phthalodialdehyde takes place, according to the author, via a concerted mechanism, while in the cationic polymerisation of *o*-vinylbenzaldehyde both mechanisms operate [53].

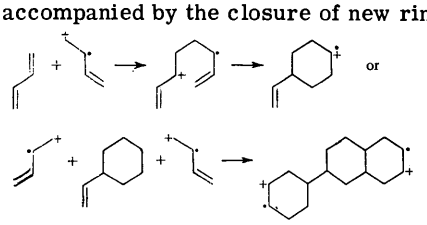
A very interesting and important aspect of the cyclopolymerisation reaction from the standpoint of the synthesis of thermostable and semiconducting materials is its employment for the synthesis of ladder and doubly cross-linked structures. Polymers of this type may be obtained both by the cyclopolymerisation of the corresponding linear polymers containing terminal multiple bonds within the framework (for example *cis*- and *trans*-polybuta-1,4-dienes [54], polyisoprenes [55,56], polyacrylonitrile [57], and polycyanoacetylene [58]) and directly by the cyclopolymerisation of diene or diyne monomers in the presence of cationic catalysts [59–65], which may be represented as follows in a general form:



The most probable mechanism of the conversion of conjugated diene monomers (or polymers) into ladder structures is one of the cationic-radical type [63,64], according to which the formation of active centres takes place via the transfer of one electron from the monomer molecule to the electron-accepting component of the catalyst A^+:



The radical-cations formed react further either with a monomer molecule or with a double bond of the polymer, this being accompanied by the closure of new rings:



It was established that identical structures are formed as a result of the cyclopolymerisation of *cis*-1,4-, *trans*-1,4-, *cis*-3,4-, and *trans*-3,4-polyisoprenes by a Ziegler-Natta catalyst [62]. At the same time, depending on the structure of the radical-cation (1,2- or 1,3-), the polymers formed have the perhydroanthracene or perhydrophenanthrene structures respectively [63,64].

In principle, cyclopolymerisation can be achieved by radical, ionic, or coordination mechanisms depending on the catalyst employed (Tables 2 and 3) and also under the influence of ultraviolet light or γ-radiation. Under these conditions, monomers containing non-conjugated double bonds show a greater dependence on the catalyst, since the different reactivities of the double bonds require more favourable conditions for the intramolecular reaction. Thus allyl acrylate reacts with azobisisobutyronitrile to form polymers containing 60 mole % of lactone groups [39], whereas anionic catalysts give rise exclusively to polymerisation involving the double bond of acrylic acid [92,93]. At the same time, a monomer such as 2,6-diphenylhepta-1,6-diene forms only a cyclopolymer in the presence of catalysts of any type [68].

Table 2. Cyclopolymerisation of symmetrical 1,6-dienes.

No.	Monomer	Polymerisation	References
1	$CH_2=CR-CH_2-CH_2-CH_2-CR=CH_2$ (R=H; Ph)	Anionic	66–69
2	$CH_2=CR-CH_2-CH_2-CH_2-CR=CH_2$ (R=COOM; COOH; COOEt, COCl; CN; $CONH_2$)	Radical Anionic	63–68
3	$CH_2=C(Ph)-CH_2-CH_2-CH_2-C(Ph)=CH_2$	Radical Anionic Cationic	68,69
4	$CH_2=CH-C(=O)-CH_2-C(=O)-CH=CH_2$	Radical Anionic	70
5	$CH_2=CH-C(=O)-O-C(=O)-CH=CH_2$	Radical	34,71
6	$CH_2-C(M)-CO-O-CO-C(M)=CH_2$	Radical	72
7	$CH_2=CH-O-CH(R)-O-CH=CH_2$ (R=H; M; *n*-Pr; Ph; CN)	Radical	73,74
8	$CH_2=CH-CH_2-\overset{+}{N}(R)(R)-CH_2-CH=CH_2$ (R=H; M).	Radical	20,75,76
9	$CH_2=CH-CH_2-N(-CH_2-CH=CH_2)-C_3H_2N_4(NH_2)_2$	γ-Irradiation Radical	77
10	$CH_2=CH-S-C(=O)-S-CH=CH_2$	Radical	78
11	$CH_2=CH-S-CHR-S-CH=CH_2$ (R=H; M; Ph)	Radical	78
12	$CH_2=C(M)-CH_2-P(=O)(R)-CH_2-C(M)=CH_2$ (R=Ph; M; Et)	Radical	79
13	$CH_2=CH-CH_2-M(R)(R)-CH_2-CH=CH_2$ (M=Sn; Ge; Si; R=M, Et; Ph)	Ziegler-Natta catalyst	80–82

Usually the cyclopolymerisation of monomeric compounds is carried out in an emulsion or in dilute solutions (at a concentration of about 0.1 M), which tends to increase the yield of soluble polymers; only a few examples of the cyclopolymerisation of monomer in the solid state are known [83].

Interesting results have been obtained in the study of the controlled and directed cyclopolymerisation of butadiene [89] and the anhydride of methacrylic acid [93,94] with radical sensitisation of the process. On the basis of data for the mechanism of free-radical polymerisation at different temperatures and after a comprehensive investigation of the specimens obtained [95–97], it was concluded that the intermolecular stage of the cyclopolymerisation process takes place stereoselectively. Reaction temperature and the predominance of one of the pyramidal structures of the strained cyclic radical formed are then of decisive importance; the axial mode of addition leads to syndiotactic stereoregularity which in the ideal case involves the presence of *ddll*-sections throughout the chain [98].

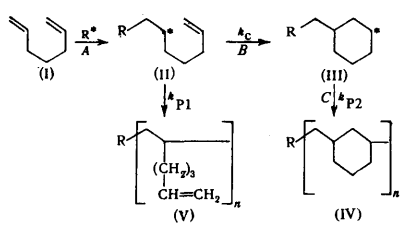
Table 3. Radical cyclopolymerisation of asymmetric dienes.

No.	Monomer	References
1	$CH_2=CH-CH_2-O-C(=O)-CH=CH_2$	83,84
2	$CH_2=CH-CH_2-O-C(=O)-CH=CHR$ (R=COOH; COOM; M)	37,85–88
3	$CH_2=CH-CH_2-NH-C(=O)-C(R)=CH_2$ (R=H; M)	84
4	$CH_2=CH-CH_2-NH-C(=O)-CH=CH-CH_3$	38
5	$CH_2=CH-O-C(=O)-CH=CH-Ph$	88,89
6	$CH_2=C(M)-C(=O)-O-C(=O)-CH=CH-M$	89
7	$CH_2=CH-O-C(=O)-CH=CH-M$	86
8	$CH_2=CH-CH_2-O-SO_2-CH=CH_2$	90,91

Numerous studies, particularly on cationic and radical systems, have been undertaken to elucidate the cyclopolymerisation mechanism. Nevertheless there is at present no theory which would yield a clear explanation of the alternation of intramolecular and intermolecular "cyclopolymerisation" steps. The latest advances in the field of anionic cyclopolymerisation and their comparison with the results quoted in a number of publications concerning radical and cationic systems, enabled Butler and coworkers [7] to make certain generalisations concerning the cyclopolymerisation mechanism.

In a general form, the cyclopolymerisation mechanism can be represented by the following scheme:

Scheme 1



where R* may be a radical, cationic, or anionic catalyst.

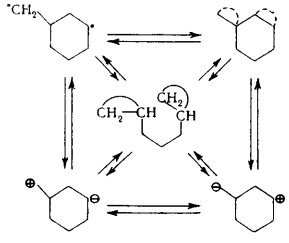
The initiator R* reacts with the terminal carbon atoms of the diene yielding the structure (II), the remaining double bond of which is involved in a further intramolecular cyclisation. The cyclic structure (III) then reacts intermolecularly with another diene molecule, this being continued until the formation of the polymer (IV). Nor can one rule out the possibility of the conversion of structure (II) via intermolecular propagation into a linear polymer (V). Therefore the most important factors here are the stability of structures (II) and (III) and the relative rates of reactions B and C.

Evidently, if the intramolecular process takes place more slowly than intermolecular reactions, the polymer will contain a large number of unsaturated groups; on the other hand, if the intramolecular process is faster than the intermolecular process, a linear and saturated polymer is obtained. It was found that the cyclisation constant k_c is then independent of the concentration of monomers and the degree of cyclisation of the polymer is determined by the ratio k_c/k_p.

Statistical calculations on the cyclopolymerisation reactions carried out by Butler and Raymond [99] for 1,6-dienes selected as model compounds showed that theoretically the monomer concentration required for the attainment of 95% cyclisation must be reduced to 0.10 M. However, in practice, polymers with 95–100% cyclisation have been obtained at a monomer concentration of 1.9–8.0 M. To account for this contradiction, the authors proposed two schemes taking into account electronic effects and steric factors; however, none of these can provide an answer to questions such as, for example, why the activation energy for cyclisation is equal to or greater than the activation energy for linear chain propagation and why the reactivity of diolefinic monomers is frequently higher than that of the analogous mono-olefins.

Therefore the only possible conclusion has now been reached that steric and entropy effects, the probabilities of the intramolecular and intermolecular steps, thermodynamic stability, and electronic effects in the transition states make a contribution to the cyclopolymerisation mechanism. The ease of cyclisation may be due to the electronic interaction between the double bonds of the 1,6-dienes or between the reaction centres formed on attack by the sensitiser and the intramolecular double bond, as can be seen from the scheme below [3,100]:

Scheme 2



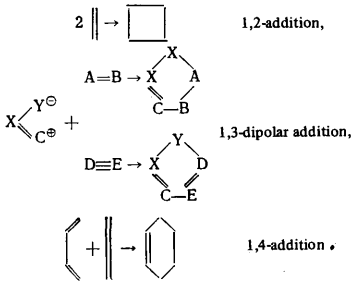
The steric resonance interaction, which constitutes the driving force of the cyclopolymerisation reaction, leads to a bathochromic shift in the ultraviolet spectra.

Similar investigations carried out on allylsilanes showed that the magnitude of the shift is satisfactorily consistent both with calculations by the molecular orbital method and with experimental observations on the polymerisation of diallyl-, [80,81,101] triallyl- and tetra-allyl-silanes [102]. The activation energy for the cyclopolymerisation of allylsilanes calculated per double bond is 9 kcal mole^{-1}. [103]

Further development of hypotheses concerning the cyclopolymerisation mechanism involves the accumulation of new data in the field of anionic processes and also the verification with the aid of new experimental techniques of the results obtained in radical and cationic systems.

III. POLYCYCLOADDITION

The use of cycloaddition reactions, which are well known in organic chemistry, for the synthesis of polymers may be regarded as a further development of methods for the synthesis of macromolecules [15];



The 1,2-addition reactions are little used in the synthesis of polymers owing to difficulties in the synthesis of the monomers and because the strain in the resulting cyclobutane ring gives rise to instability of the polymers.

1. 1,3-Dipolar Cycloaddition

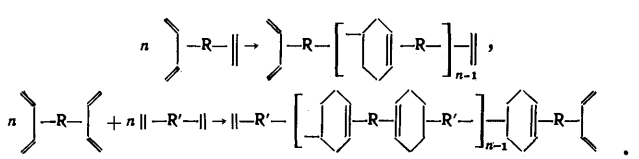
1,3-Dipolar cycloaddition reactions have found some application in the synthesis of polymers, since the bifunctional monomers are relatively easily synthesised and the majority of dipolar addition reactions take place quantitatively. Moreover, the above method is interesting because it makes it possible to introduce into the polymer chain the greatest variety of five-membered heterocyclic systems and is frequently used in those cases where other methods are less effective; if the dipolarophiles contain triple bonds, for example acetylenes or nitriles, and the dipole has an atom Y with a lone electron pair, the resulting heterocycle is aromatic (it includes a π-electron sextet), which is the reason for the high thermal stability and heat resistance of the corresponding polymers.

The main types of polymers synthesised by the 1,3-dipolar addition reaction are listed in Table 4. It is noteworthy that the formation of a mixture of polymeric products with different positions of substituents in the heterocycles is possible in many cases.

2. The Diels–Alder Reaction

The Diels–Alder reaction is achieved by the interaction of a diene and a dienophile; the latter include maleic anhydride, acrolein, vinyl monomers, and also various quinones. The Diels–Alder polymerisation can be achieved starting with monomers containing in a single molecule both diene and dienophile functional groups or via

the copolymerisation of bisdienes with bisdienophiles according to the following mechanisms [11]:



Polymers with high softening temperatures have been obtained by the interaction of 1,5-di-(9-anthryl)penta-1,4-diene and anthryl azine with benzidine-bismaleimide [11]:

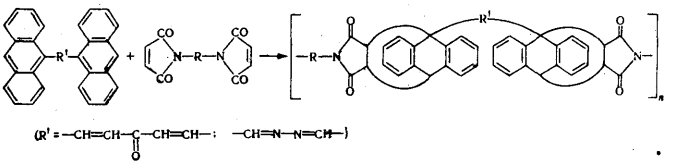
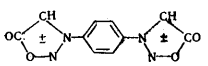
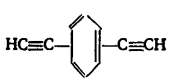
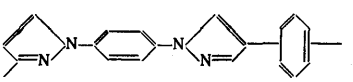
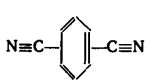
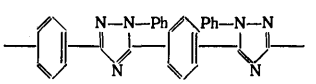
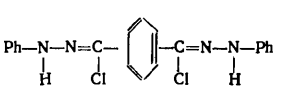
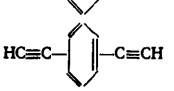
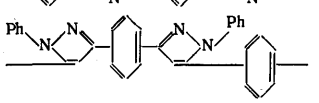
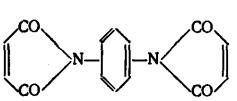
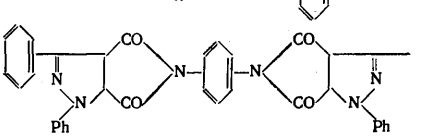
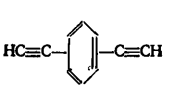
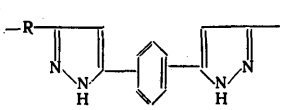
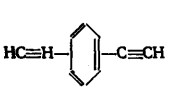
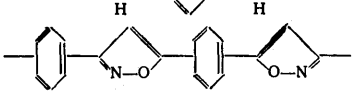
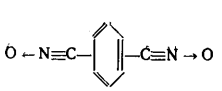
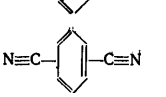
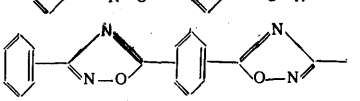
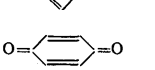
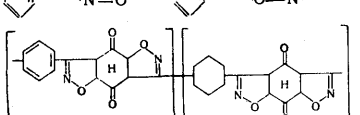
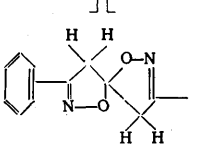
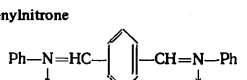
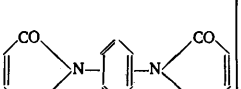
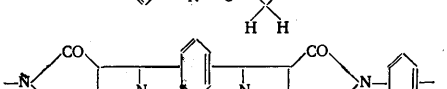
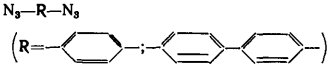
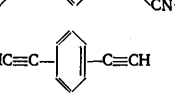
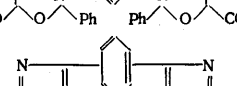
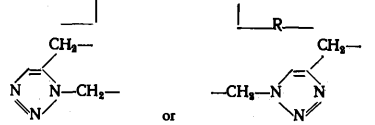
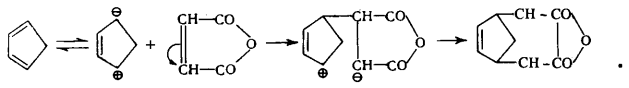


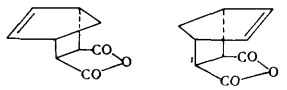
Table 4. Types of polymer synthesised by the dipolar 1,3-addition reaction.

1,3-Dipole	Dipolarophile	Polymer unit	References
Bis-sydnones 			104 105
Bisnitrileimines			
			106
			
Bisdiazoalkanes $N_2CH—R—CHN_2$ $R=(CH_2)_4; (CH_2)_3; C_6H_4.$			107
Bis(nitrile oxides)			
			108
			
	$H_2C=C=CH_2$		
Bisphenylnitrone 			109
Diazides $N_3—R—N_3$ 			110
$HC\equiv C—CH_2—CH_2—N_3$			
(mixed dipole-dipolarophile)		 or	111

Although the Diels–Alder polymerisation includes reactions of unsaturated compounds and the resulting polymers do not have a structure typical for condensation products, the synthesis of the polymer itself resembles polycondensation. In a general form, this reaction involves the π electrons of both components and the formation of a dimeric product according to the mechanism



In the interaction of cyclopentadiene with maleic anhydride, two forms of addition are possible, but the *endo*-form is produced preferentially [11]:



exo-form *endo*-form

In many cases, the synthesis of polymers with regular structures has been achieved by the Diels–Alder reaction [11]. Thus the polymers obtained by the reaction of cyclopentadienes, α-pyrones, or thiophen dioxides with bismaleimides contain bicyclo[2,2,2]octene rings in which the imide groups are in the *exo*-position. Even reactions in which both these forms are produced should lead to chains with a certain degree of order in the distribution of *endo*- and *exo*-groups in relation to the chain.

Polymers obtained by the Diels–Alder reaction are as a rule amorphous, but their amorphous nature does not rule out the possibility of stereoregularity [11].

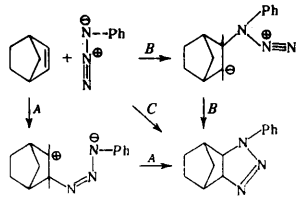
Kinetic studies have shown that polymerisation includes a number of individual reactions and is a stepwise and not a chain process. Therefore, the equation for second-order reactions $-dc/dt = KC^2$, where C is the concentration of the terminal diene and dienophile groups, should hold for the Diels–Alder reaction. The decrease of the rate on dilution of the solutions and on decrease of the molecular mobility of the reactants is typical for the Diels–Alder reaction.

The degree of polymerisation in the Diels–Alder reaction depends on its duration, since at the beginning oligomers accumulate in the reaction mixture and are gradually converted into products with a higher molecular weight. However, one should bear in mind that the Diels–Alder reaction is reversible and that at high temperatures the polymeric products may decompose into dienes and dienophiles. It is postulated that the dissociation takes place more readily in the centre of the molecular chain than at its ends, which leads to a narrowing of the molecular weight distribution [11].

Despite the fact that in many cases a biradical mechanism has been postulated for the Diels–Alder reaction [113], the vast majority of experimental data are consistent only with a synchronous mechanism [114] of the $[\pi 4 + \pi 2]$-cycloaddition type with retention of orbital symmetry [115,116].

The mechanism of the 1,3-dipolar cycloaddition reaction involving polymers has not yet been investigated. However, since there is sufficient information about 1,3-dipolar addition reactions of low-molecular-weight substances, certain comparisons may be made and conclusions reached [112]. 1,3-Dipolar polyaddition has much in common with polymerisation via the Diels–Alder reaction: it is an example of ionic [4 + 2]-cycloaddition, because, although the molecules of 1,3-dipolar compounds involved in cycloaddition reactions are formally neutral, they usually behave as three-orbital 4π-electron species [117].

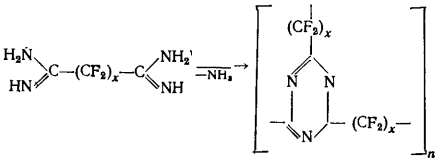
Analysis of 1,3-dipolar addition [115–118] and Diels–Alder reactions on the basis of the rule of conservation of orbital symmetry [119] has demonstrated the similarity of these two processes, which makes it possible to classify the former as pseudo-Diels–Alder reactions and suggests that they have similar kinetics and mechanism. Of the three theoretically possible mechanisms for the addition of a 1,3-dipole to double and triple bonds, illustrated for the interaction of phenyl azide with bicycloheptene as an example, the most likely is mechanism (*C*) with cyclic electron transfer and simultaneous formation of two new bonds [117]:



[(*A*) the positive end of the dipole initiates attack; (*B*) the negative end of the dipole initiates attack; (*C*) the addition takes place simultaneously]. According to mechanism (*C*), the synchronous electron shift leads to the formation of two new σ bonds and enables all three nitrogen atoms to reach octet stability without carrying a formal charge.

IV. POLYCYCLOTRIMERISATION

Polycyclotrimerisation can be achieved both as a polycondensation and a polymerisation process, which results in the formation of carbocyclic or heterocyclic polymers. The polycyclotrimerisation reaction was used for the first time to synthesise polymers by Brown [120–122], who described the polycondensation of diamidines with evolution of ammonia and the formation of cross-linked polytriazines:

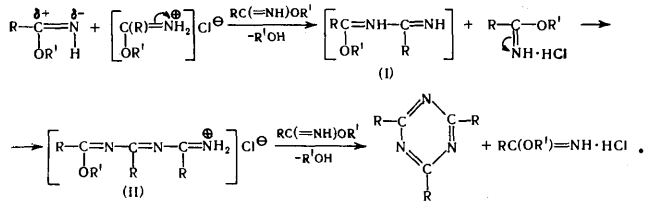


The addition of monoamidines appreciably suppresses the structure-formation process but nevertheless does not altogether rule it out owing to the considerable difference between the reactivities of mono- and bi-functional monomers.

In the course of further studies, the characteristics of this reaction and of the polycyclotrimerisation of fluorinated and non-fluorinated iminoesters were investigated in the presence and absence of catalysts, namely the dependence of the thermal degradation and other properties of the polymers obtained on the nature of the group linking the triazine rings; much attention has been devoted to problems of the processing and applications of triazine rubbers [123–134].

Yakubovich et al. [131] believe that the condensation of iminoester groups into triazine rings proceeds via a series of consecutive stages leading to the formation of a

linear "dimer" (I) and "trimer" (II). The resulting hydrochloride of the linear "trimer" (II) cyclises into the more stable *s*-triazine systems via the mechanism [135]



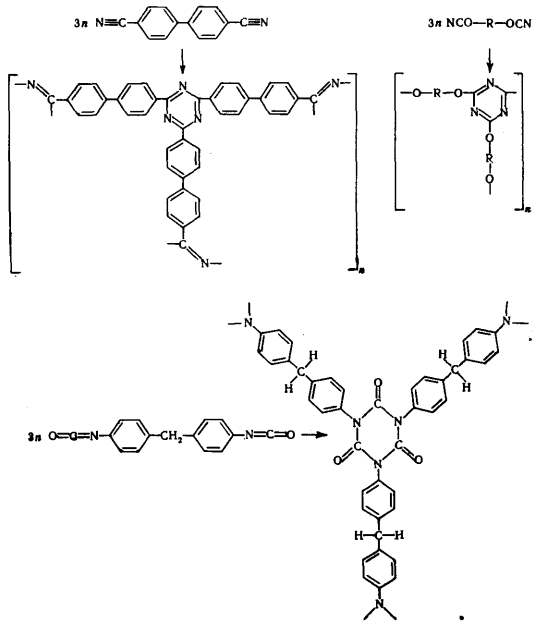
Presumably the electrophilic properties of the carbon atom in iminoesters are insufficient to ensure the effective addition of a second iminoester molecule to the C=N double bond; therefore the cyclisation of the free bases of the iminoesters takes place only in the presence of the iminoester hydrochloride, in which the electrophilic properties of the carbonyl carbon atom are enhanced owing to the presence of 'onium nitrogen and the associated shift of the π-electron density of the double bond:



The substitution of hydrogen atoms in the alkyl group of bisiminoesters by fluorine increases the electrophilicity of the carbonyl carbon atom to such an extent that the triazine ring is formed also in the absence of a catalyst [134]. In order to obtain linear polytriazines under these conditions, it is necessary that one position in the triazine ring should be substituted by a non-reactive side group and the remaining two should be involved in the formation of the polymer chain.

Examples of polycyclotrimerisation are provided by the formation of polymers with triazine rings from aromatic dinitriles, aryl cyanurates, or aryl di-isocyanates [14].

Scheme 3

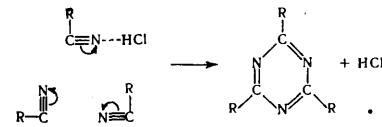


The reason for the tendency of compounds containing C=N bonds to form stable cyclic trimers is that, on conversion of monomers into trimers, the enthalpy of the π bond is lost; moreover, the cyclic trimer is stabilised owing to the combination of the most favourable valence angles (120°) and the planarity of the resulting ring, which makes possible the existence in the trimer of a stable aromatic system [136-139]. The inclusion of stable aromatic systems between triazine rings is responsible for the high thermal stability of the polymers [138].

The cyclotrimerisation of nitriles may be accelerated by many catalysts, for example, by the halides of coordination-unsaturated metals. The presence of a lone electron pair and of π bonds in the C≡N group promotes the formation of highly electrophilic molecular complexes with Lewis acids. It is suggested that the addition of more than one equivalent of the electrophilic compounds to a nitrile is due to the formation of the so called π complexes [140].

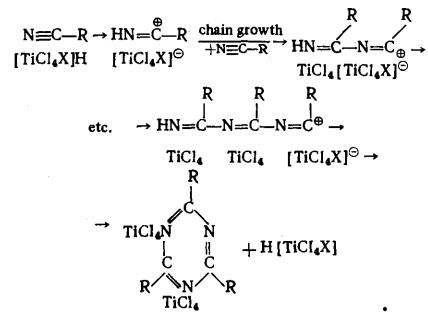
Hydrogen halides are used most often among compounds inducing the cyclotrimerisation of nitriles [141], but reactants such as sulphuric and chlorosulphonic acids, Lewis acids, and others can also serve as catalysts [142-145]. The ease of formation of the *s*-triazine ring in the presence of HCl is probably due to the possibility of a cyclic electron transfer via Scheme 4: [146,147]

Scheme 4



According to Scheme 4, both the free nitrile and its complex with the hydrogen halide is involved in the formation of triazines.

Interesting results have been obtained by Kargin and coworkers [148-153] in a study of the mechanism and kinetics of the polymerisation of benzonitrile with compounds such as $TiCl_4$, $ZnCl_2$, and BF_3. [149] They also showed that triphenyltriazine is an intermediate in the formation of a linear polymer with a polyene structure and that the complex $[TiCl_4X]H$, formed in the interaction between the complex-forming agent and proton-containing additives, serves as a centre for chain initiation [152]:



Petrov et al. [154] studied the kinetics of the cyclotrimerisation of di-isocyanates by infrared spectroscopy using as a test object the polymer obtained by the interaction of one mole of low-molecular-weight polybutadiene (mol. wt. 4000) containing terminal OH groups with 2 moles of 2,4-tolylene di-isocyanate in the presence of a catalytic system including glycidyl phenyl ether and dimethylbenzylamine in different proportions. It was shown that the cyclotrimerisation of isocyanate groups corresponds to a quasi-monomolecular reaction up to 70–90% conversion; the rate of cyclotrimerisation is directly proportional to the product of the initial concentrations of the tertiary amine and the epoxyalkane. The author suggested that the cyclotrimerisation reaction is a special case of anionic polymerisation [154].

The results have been explained in terms of the stepwise Beitchman mechanism [155], according to which the addition of the first, second, and third isocyanate (M) molecules to the catalytic complex (N) takes place in the same way:

$$N + M \xrightarrow{k} NM,$$

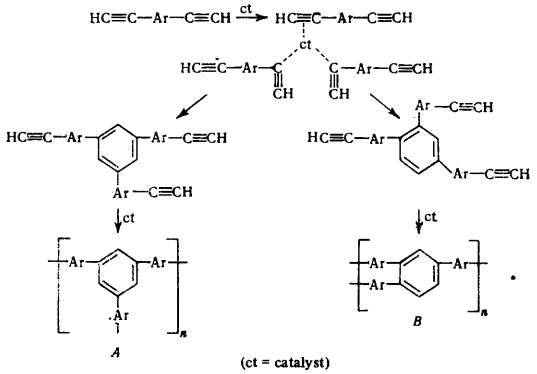
$$NM + M \xrightarrow{k} NM_2,$$

$$NM_2 + M \xrightarrow{k} M_3 + N.$$

Although the closure of the isocyanate ring, accompanied by the elimination of the catalyst, is most likely in the trimer stage, in principle the formation of a linear polymer or the arrest of reaction at the dimer stage are possible.

Korshak, Sergeev, and coworkers [156,157] achieved the polycyclotrimerisation of diethynyl compounds in bulk and in solution in the presence of complex catalyst which consisted of various complexes of cobalt, nickel, and other transition metals capable of catalysing the cyclisation of acetylenes into benzene and its derivatives. The overall mechanism of the polycyclotrimerisation of diethynyl compounds may be regarded as involving the consecutive trimerisation of ethynyl groups leading to chain propagation, branching, and cross-linking (see Scheme 5).

Scheme 5



(ct = catalyst)

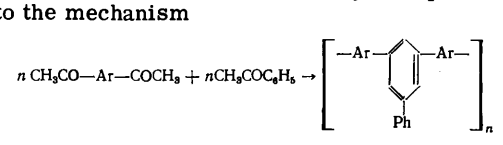
The study of the infrared and NMR spectra showed that polycyclotrimerisation results in a decrease of the intensity of the absorption band corresponding to the stretching vibrations of the ≡C–H linkages (3300 cm^{-1}) and an increase of the vibration frequency of the hydrogen atoms linked to the benzene ring.

The formation of 1,3,5- and 1,2,4-substituted benzenes depends on the nature of the catalyst metal and the ligand [156,157]. The use of a mixture of diethynyl and monoethynyl compounds make it possible to regulate the degree of branching of the polymer formed:



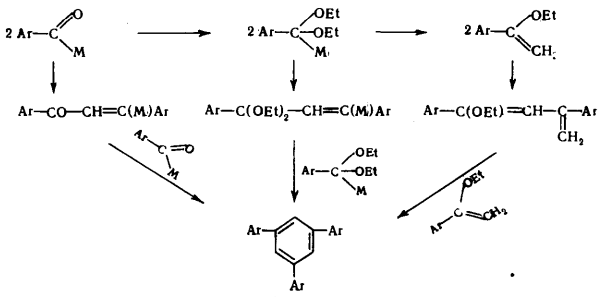
On heat treatment, oligomeric polycyclotrimerisation products are converted into an infusible and insoluble state.

Korshak, Teplyakov, and coworkers [158,159] proposed a new method for the synthesis of polyphenylenes via the polycondensation of aromatic diacetyl compounds according to the mechanism



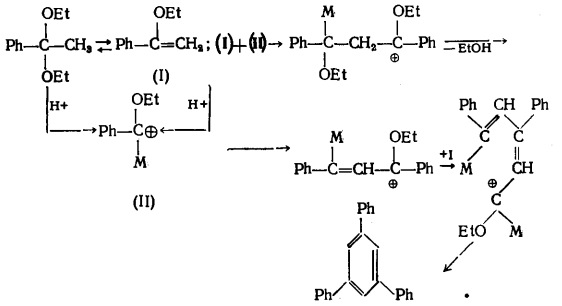
However, as in the trimerisation of acetylenic compounds, it was found that the use of diacetyl monomers alone leads rapidly to the formation of three-dimensional products. Therefore, one usually employs equimolar mixtures of di- and mono-acetyl compounds, although in this case too gel formation is observed in the course of the reaction.

The authors showed that the formation of the benzene ring is a fairly complex process including as an intermediate stage the crotonic condensation of the acetyl groups, resulting initially in the formation of a dimer and then a trimer, the intramolecular cyclisation of which yields 1,3,5-substituted benzene rings. The catalytic effect on the reaction by ethyl orthoformate, which apparently promotes the conversion of acetyl compounds in an acid medium into more reactive ketals, has been noted. In this case, the mechanism of the possible fundamental steps in the formation of polyphenylenes can be represented as follows [158]:



A detailed study has been made of the cyclocondensation of acetophenone ketal, which can serve as a model for the synthesis of polymers. Mass-spectrometric analysis established that a certain amount of α-ethoxystyrene, dypnone [1,3-diphenyl-2-buten-1-one], and 1,3,5,7-tetraphenylcyclo-octatetraene is formed in the course of the reaction together with triphenylbenzene [159]. Kinetic investigations established that the cyclocondensation of acetophenone ketal is described by the equation for second-order reactions with a rate constant of $(1.2-1.4) \times 10^{-1}$ litre $mole^{-1}$ min^{-1} at 20°C.

The authors proposed the following mechanism for the condensation of acetophenone ketal on the basis of the results obtained:



The employment of diacetylarylene bisketals together with acetophenone ketal makes it possible to achieve polycondensation and to obtain soluble linear polyphenylenes consisting of oligomers with a molecular weight up to 3000. The oligophenylenes are hardened by heat treatment in an inert atmosphere at 300°C using toluene-*p*-sulphonic acid as the catalyst; the hardened polyphenylenes are infusible and insoluble; they are decomposed vigorously in air at about 400°C. The infrared spectra

of the heat-treated polyphenylenes show no absorption whatever due to the vibrations of the terminal ketal groups.

V. POLYHETEROCYCLISATION

Polyheterocyclisation is a typical polycondensation process, which can be achieved in different ways. (1) In two stages (the first stage involves the formation of linear polymers containing in their macromolecules fragments capable of cyclisation and the second stage, the cyclisation proper, leads to a cyclochain polymer with repeating heterocycles in the chain); (2) in one stage—in polyphosphoric acid (PPA). The most interesting polyheterocyclisation products from the standpoint of thermal stability and heat resistance are polyheteroarylenes—polymers containing only aromatic carbocyclic and heterocyclic groups in the macrochains.

Certain polyheteroarylenes can be formed also on direct fusion of the starting compounds; however, this method is not preparatively useful, since it requires a high temperature at which secondary processes (degradation, cross-linking) may occur in the polymers and alter their properties.

The majority of polyheteroarylenes can be obtained by both methods; each of these has its advantages and disadvantages, largely associated with the properties of the final product. Since the majority of polyheteroarylenes do not melt and do not dissolve in the usual organic solvents, an advantage of the two-stage method is the formation in the first stage of soluble prepolymers, which can be worked into finished articles by the usual methods and then cyclised by heat treatment.

An advantage of the synthesis in PPA is primarily the occurrence of the process in a single stage, its relative simplicity, cheapness, and the ready availability of the starting compounds. Moreover, PPA, which provides a unique combination of the properties of an effective solvent for polymers, a proton donor (this promotes the condensation), and a cyclodehydrating agent, frequently makes it possible to synthesise polymers with a higher molecular weight and with a higher degree of cyclisation. In the two-stage process, the cyclisation usually occurs in the solid phase and, as the reaction proceeds, the macromolecular chains become increasingly rigid, which greatly hinders the occurrence of total cyclisation; PPA, which in this case behaves as a plasticiser, promotes the attainment of a higher degree of cyclisation.

A wide variety of different classes of polyheteroarylenes have been obtained by the above methods and the most important among them are the following: (1) *polyazoles*—polymers containing repeating five-membered heterocycles in the macromolecules: oxadiazole, triazole, pyrazole, thiadiazole, and other units; (2) *polybenzazoles*

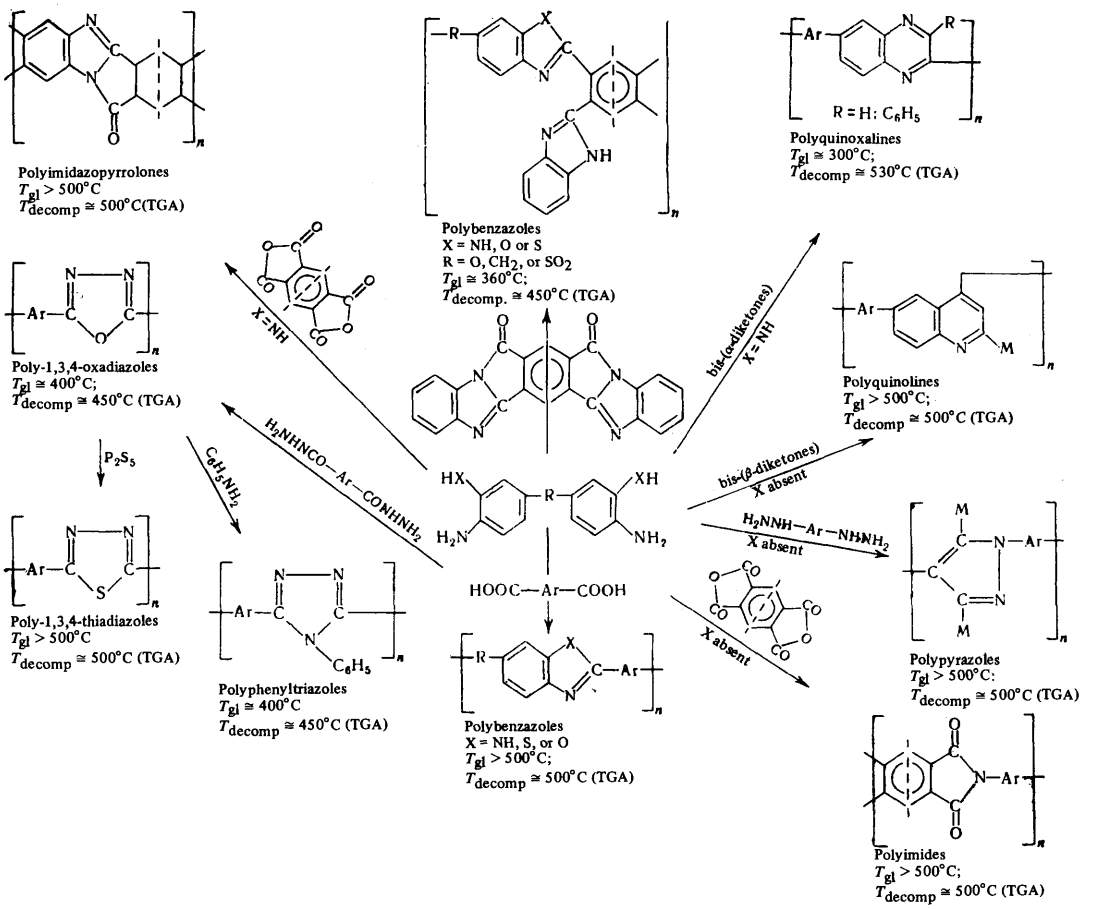


Figure 1. Scheme for the formation and main thermal characteristics of the principal types of polyheteroarylenes.

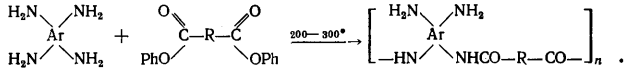
and *polybenzazines* —polymers containing condensed heterocycles: benzimidazole, benzoxazole, benzothiazole, benzimide, indole, quinoline, quinoxaline, benzoxazine, and other units; 3) ladder polymers of different structures.

Fig. 1 presents a general scheme for the formation of the main polyheteroarylenes indicated above and some of their thermal characteristics.

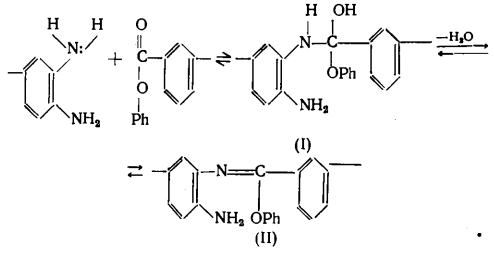
1. Two-stage Method of Synthesising Polyheteroarylenes

The first stage of this process has been investigated in many systems and such studies have led the majority of investigators to the conclusion that at this stage the reaction is reversible and obeys relations characteristic of equilibrium polycondensation [160–165]. Since the second stage is the cyclisation proper and the properties of the final polyheteroarylenes are to a large extent determined by the structure of the prepolymers, we shall consider in this section also the mechanism of the reactions occurring in the first stage.

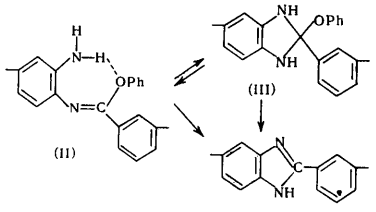
According to the literature [166,167], the formation of polybenzimidazoles on interaction of 3,3′-diaminobenzidine with diphenyl esters of dicarboxylic acid takes place via the formation of a polyaminoamide as an intermediate:



However, Wrasidlo and Levine [168] believe that such interaction begins with the nucleophilic attack by the amine on the carbonyl carbon atom of the diphenyl ester, leading to the formation of an intermediate aldol type product (I), which after dehydration gives rise to a new intermediate with the structure of a Schiff base (II):

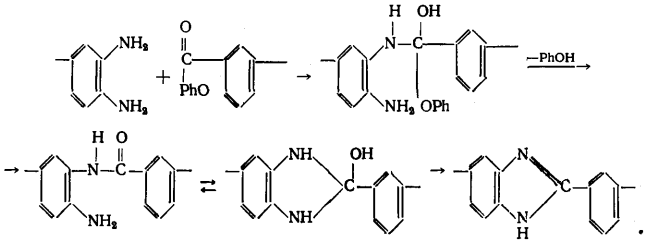


The *syn*-form of the intermediate (II) can produce intramolecular hydrogen bonds, which promote the intramolecular formation of phenol and prevent the formation of cross-linked and branched structures. The authors postulate the possibility of an equilibrium between the intermediate (II) and the benzimidazole structure (III):

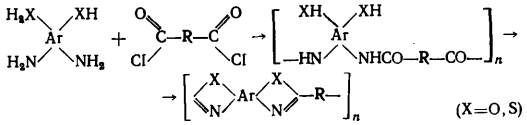


The consecutive elimination of phenol from structures (II) and (III) leads to the final benzimidazole. The electronic absorption spectra of the prepolymer and the fact that water is formed before the phenol are quoted in support of the proposed mechanism.

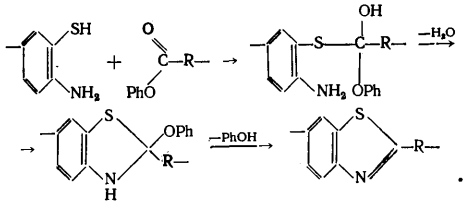
However, Grey et al. [169], who studied the reaction in a flow system in contrast to the earlier investigators, demonstrated on the basis of spectroscopic data and elemental analysis that water and phenol begin to form simultaneously and that half the theoretical amount of water and the entire phenol are produced in the first stage and only water in the second stage. This led them to the conclusion that the reaction intermediate has a hydroxyimidazoline structure formed via the following mechanism:



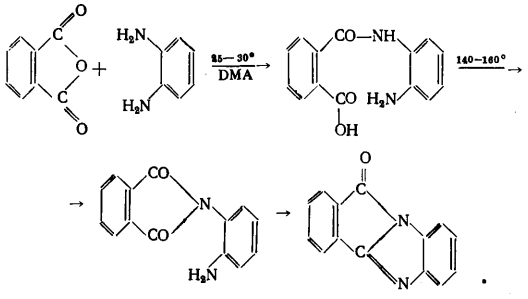
Many workers believe that polybenzoxazoles [170–172] and polybenzothiazoles [173] are formed via a polyhydroxamide and a polymercaptamide respectively as intermediates in the first stage:



It has been suggested that the reaction of 3,3′-dimercaptobenzidine with diphenyl esters in diethylaniline solution proceeds via a different mechanism [174]:



The synthesis of ladder polymers (for example pyrrone type polymers) by the two-stage method proceeds via the formation of a polyaminoamidoacid in the first stage, which has been demonstrated convincingly by Colson et al. [175], using NMR, for the reaction of phthalic anhydride with *o*-phenylenediamine:



The study of the reaction of bis-(β-diketones) with dicarboxylic acid dihydrazides by Korshak and coworkers [176] in order to synthesise polypyrazoles showed that polyacylhydrazones are formed as intermediates in the first stage. The kinetic data obtained by the authors for this stage contradict the earlier idea according to which the interaction of amines with carbonyl compounds is regarded as a bimolecular process, the rate-limiting stage of which is

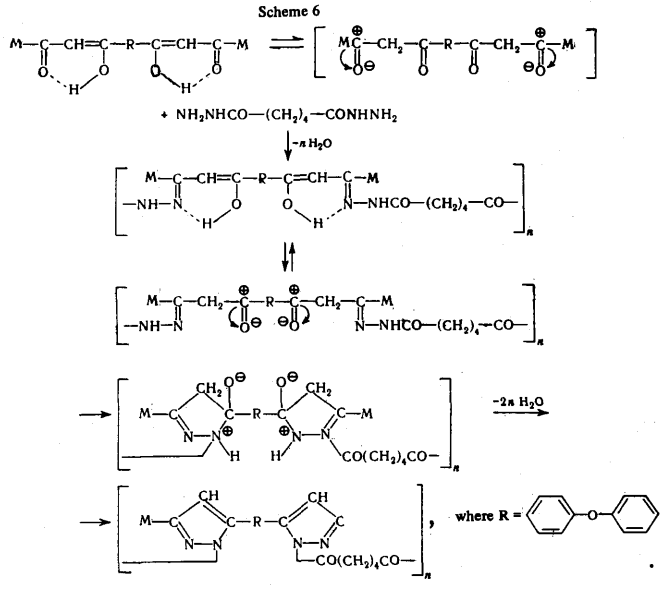
the formation of an intermediate adduct [177,178]. The interaction of 4-acetoacetylphenyl ether and adipodihydrazide under the chosen conditions was irreversible and obeyed the equations for first-order reactions. The activation energy was 17 kcal mole^{-1} and at first sight greatly exceeded the usual activation energy for a keto–enol transformation. Therefore, the hydrogen bond energy in 4-acetoacetylphenyl ether was determined by 1 H NMR and was indeed found to be 23 ± 4 kcal mole^{-1}. Such unusually marked stabilisation of the intramolecular hydrogen bond is probably due to the conjugation of the enol ring with the benzene rings, as in benzoylacetone and dibenzoylmethane [179].

On the basis of their results, the authors proposed a mechanism for the formation of polypyrozoles according to which bis-(β-diketones) and the intermediate hydrazones react in the keto-form (see Scheme 6).

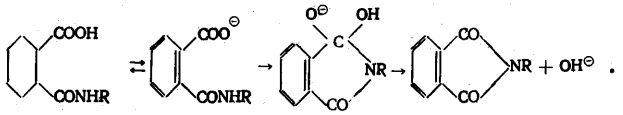
The second stage in the synthesis of polyheteroarylenes—dehydrocyclisation—consists in the intramolecular formation of water from the intermediate product with formation of a cyclochain polymer and may be achieved both in solution and in the solid phase. These processes are being vigorously investigated since they have a direct influence on the properties of the polymers [180–194].

A study of the kinetics of the imidisation of a polyamidoacid in solution in dimethyl acetamide at 80°C on the basis of the amount of water formed, both chromatographically and from the change of the absorption intensity in the region of 1780 cm^{-1}, showed that the process is first-order with a rate constant $k = 3.87 \times 10^{-3}$ litre mole^{-1} s^{-1}. The reaction is very rapid and after 11 min the degree of imidisation is 98.5%. [180] The reaction rate depends on the nature of the diamine and the dianhydride: polyamidoacids comprising more basic diamines and aromatic dianhydrides are cyclised more readily.

Scheme 6



It was observed that the cyclisation of a polyamidoacid in the form of the ammonium salt proceeds much faster (by a factor of 5–10) compared with the cyclisation of the free polyamidoacid. Therefore, it has been suggested that the mechanism of the cyclisation reaction includes a stage in which the carboxy-group is ionised [184]:



On the other hand, the cyclisation of the methyl ester of a polyamidoacid proceeds much more slowly than that of the acid itself [187], which constitutes indirect confirmation of the above hypothesis.

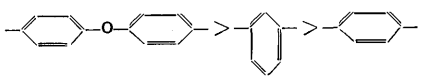
A characteristic feature of the kinetic curves for the cyclisation of polyamidoacids is the presence of two stages, the first of which corresponds to rapid cyclisation and the second to a very slow process. The activation energies for the two stages are almost the same, but the activation entropy for the second stage is significantly higher [184]. If the water formed in the cyclisation process is not removed from solution, then hydrolytic cleavage of the macromolecules and a decrease of the molecular weight of the polymer are possible at the reaction temperature [180]. Therefore, in solid-phase cyclisation, which takes place at higher temperatures (250–300°C), it is necessary to remove water rapidly from the reaction zone; consequently, the cyclodehydration of solid prepolymers is carried out in thin layers *in vacuo* [183–187].

The studies showed that the mechanism of solid-phase cyclisation is more complicated in solution. Regardless of the prepolymer cyclised (polyamidoacid, polyhydroxamide, polyhydrazide, and others), the kinetics of these reactions have the following common feature: regardless of the fact that all such reactions are unimolecular and are treated as first-order processes, the rate constant calculated from the first-order kinetic equation decreases monotonically with conversion. Thus, with increase of the degree of cyclisation of a polyamidoacid from 0.2 to 0.8, the absolute reaction rate constant increases by a factor of 10–12. The decrease of the imidisation (and in general cyclisation) rate constant with increase of the degree of reaction may be accounted for by the fact that the energy and time parameters of the constant k in the Arrhenius equation do not remain constant in the solid-phase process [183]. The decrease of the reactivity of the macromolecules in consequence of the increased rigidity of the polymer chains and their decreased mobility with increase of the degree of cyclisation may be regarded as one of the causes of this phenomenon.

An attempt has been made to estimate quantitatively the change in mobility (increase of rigidity) of polymer chains during cyclisation using as an example the polyhydrazide obtained from the dihydrazide of 4-carboxyphenyl ether and the dichloride of diphenylphthalide-4,4′-dicarboxylic acid [188]. It was shown that the glass temperature of the resulting intermediate exceeds the experimental temperature, the solid-phase reaction is sharply inhibited and virtually comes to a stop; under these conditions, the degree of cyclisation does not reach the maximum possible value. In this case, one observes "self-inhibition" of the reaction owing to a continuous change in the mobility of the polymer chains during the solid-phase polycyclisation caused by the increase of their rigidity due to the increase in the content of cyclic fragments.

The authors suggest that the specific behaviour of these polymers is due to the non-indentity (according to the thermodynamic parameters) of the polymer chains involved in the reaction; this is responsible for the change in the reactivity of the hydrazide groups in the cyclisation [188–190].

The cyclodehydration of polyhydroxamides takes place at 250–300°C. Despite the fact that the decrease of molecular weight during cyclisation corresponds to the calculated values, amide units may persist under these conditions in the polymer, as shown by the presence in the infrared spectra of a weak absorption band at 1660 cm^{-1}. This band disappears only after heating the polymer at 420–430°C, which is accompanied by the formation of a small amount of water and carbon dioxide and the loss of solubility of the polymer in sulphuric acid [192]. The study of the kinetics of the cyclisation of polyhydroxamides showed that the chemical structure of the initial polyhydroxamide influences the rate of the process in a manner similar to that observed for other polymers: with decrease of the mobility of the macromolecular chains in the cyclisation process (i.e. with decrease of the number of units capable of rotation), the cyclisation rate constant falls and the pre-exponential factor increases. It has been established that the rate of cyclisation decreases in the following sequence as a function of the groups linking the benzoxazole rings [193]:

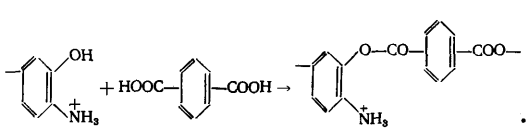


The authors suggest that the mechanism of the cyclodehydration of polyhydroxamides does not include a preliminary amide–imidoyl rearrangement, as shown by the formation of 2-phenylbenzoxazole from *o*-hydroxy-*N*-methylbenzanilide in which such tautomerism is impossible. The presence of a strong intramolecular hydrogen bond, which probably plays an important role in cyclodehydration, has been detected in the infrared spectra of *o*-hydroxamides [194].

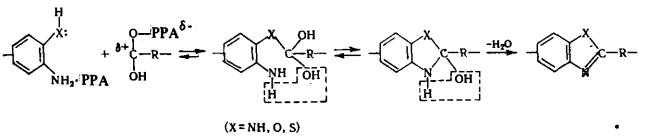
2. Single-stage Method of Synthesising Polyheteroarylenes in Polyphosphoric Acid

The elucidation of the mechanism of polyheterocyclisation in PPA was preceded by a detailed study of the acid properties of PPA itself as the P_2O_5–H_2O system [195-198] and also of the mechanism of the ring closure of a number of low-molecular-weight compounds [198,199], which led to the hypothesis that PPA acts simultaneously as a protic acid, a Lewis acid, and a phosphorylating agent [200]. This is the reason for the change in the reactivity of various compounds when the reaction is carried out in PPA.

Thus, it has been shown that, being a strong Lewis acid, PPA increases the positive charge on the carbon atom of the carbonyl group and thereby leads to an increase of its electrophilic reactivity. It is also interesting to note that, in reactions in PPA, the basicity of the hydroxy-group is higher than that of the amino-group; therefore, the reaction of bis-(*o*-aminophenols) with dicarboxylic acids in PPA involves the initial selective formation of a polyester [170]:



Taking these facts into account, Iwakura and coworkers [170] achieved for the first time the synthesis of polyheteroarylenes in PPA and proposed the following general mechanism for the formation of polybenzazoles:

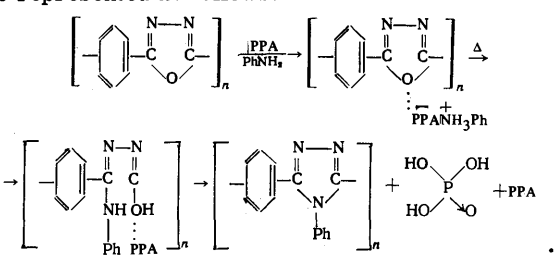


(X = NH, O, S)

It has been suggested that the intermediates formed are hydroxyimidazolines in the synthesis of polybenzimidazoles in PPA and the corresponding hydroxy-derivatives in the synthesis of polybenzoxazoles and polybenzothiazoles. It was noted that a high molecular weight is attained more rapidly in the last two cases than for polybenzimidazoles. According to the authors, this is due to the higher basicity of the hydroxy- and mercapto-groups in PPA compared with the amino-group and this is in fact the reason for the higher rate of formation of the polymer [201,202].

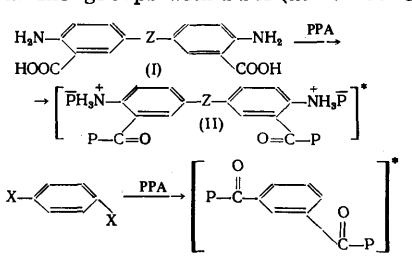
Probably the mechanism of the formation of poly-1,3,4-oxadiazoles from dicarboxylic acids and hydrazine derivatives in PPA is analogous to that quoted above [203], but this requires experimental proof.

The data obtained by Meiboom and coworkers [204] in a study of the rate of proton transfer in an acid medium to substituted ammonium ions proved to be important for the elucidation of the mechanism of their reactions in PPA. It was shown that the formation of the free base is the rate-limiting stage in this process. Later Holsten and Liliquist [205-207] determined by NMR spectroscopy the temperature range in which the aniline–PPA salt dissociates into the free acid and aniline. Accordingly, the mechanism of the formation of polyphenyltriazoles by the reaction of a polyhydrazide or polyoxadiazole with aniline may be represented as follows:



Kurihara and coworkers [208-210] made a detailed study by spectroscopic and chemical methods of the mechanism of the formation of polybenzoxazinones in PPA by the polycondensation of bisanthranilic acids and their copolycondensation with dicarboxylic acid derivatives. They demonstrated convincingly that the synthesis of polybenzoxazinones in PPA proceeds via the formation of phosphorylated intermediates in the following way.

First stage—phosphorylation of both initial compounds with formation of mixed anhydrides and the interaction of the amino-groups with PPA (at 40–80°C):

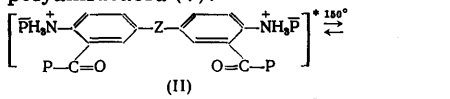


where Z = CH_2 or O, X = COOH, COCl, CN, C(=NH)OR,

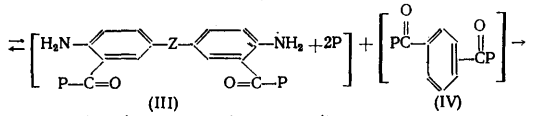
COOR, $CONH_2$, or CHO, R = CH_3, C_2H_5 or C_6H_5,

P = $H[OP(OH)_n]O$, and [ ]* = activated complex.

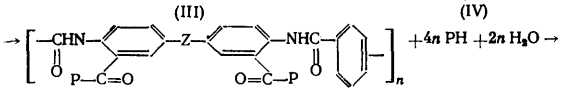
Second stage—the formation of the polyamidoacid (V). At 150°C the salt (II) dissociates and an equilibrium is established between the salt and the free amino-form of the phosphorylated product. The reaction is initiated by the nucleophilic attack by the free-amino groups on the carbonyl group of the mixed anhydride and leads to the formation of the polyamidoacid (V):



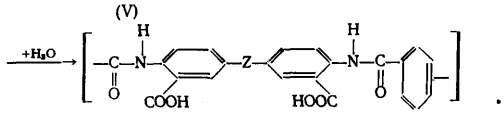
(II)



(III) (IV)

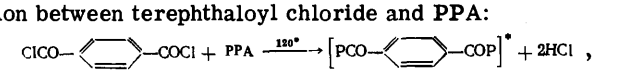


(V)



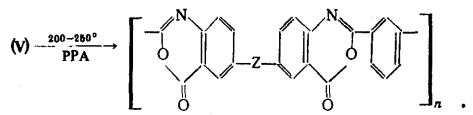
(VI)

The presence of the mixed anhydride (IV) in the reaction mixture has been demonstrated by carrying out the reaction between terephthaloyl chloride and PPA:



which resulted in the formation of a stoichiometric amount of hydrogen chloride. The carbonyl group in such a mixed phosphorylated anhydride is more sensitive to nucleophilic attack by amino- or phosphoramido-groups. The presence of free NH_2 groups, which appear as a result of the dissociation of the amine salt (II) in PPA, has been demonstrated by NMR. The polyamidoacid (V) was isolated from the reaction mixture and characterised by elemental analysis and infrared spectroscopy.

Third stage—cyclodehydration in PPA. This occurs on further heating and leads to polybenzoxazinones:



(VII)

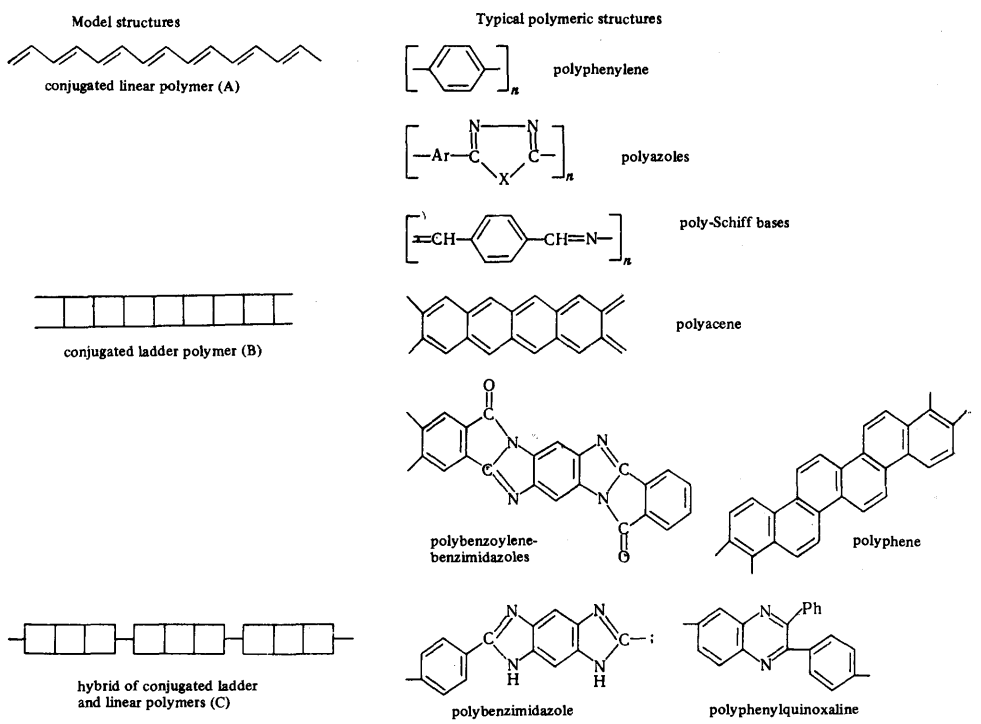
VI. LIMITS OF THE APPLICABILITY OF THE POLYCYCLISATION METHOD

Examination of the above data permits the following conclusions.

1. Despite the apparent wide variety of methods described, they are all based on well known polymerisation and polycondensation processes.
2. Methods leading to polymers with continuous conjugation or pseudo-conjugation of the aromatic (carbocyclic and heterocyclic) structural skeleton, i.e. polyheterocyclisation, polycyclotrimerisation, and 1,3-dipolar addition, are the most suitable for the synthesis of thermostable and heat-resistant organic polymers.
3. The two-stage method of synthesising polyheteroarylenes, whereby it is possible to obtain in the first stage soluble polymers capable of being worked, has nowadays been developed to the greatest extent.

All the above types of polyheteroarylenes can be represented by models[211] (see Scheme 7).

Scheme 7



The presence in the polymer macromolecules of aromatic carbocyclic and heterocyclic groups alone, which are responsible for the rigidity of the main chain and the strong interchain interaction, should lead to high softening temperatures (heat resistance) and resistance to high temperatures (thermal stability) and chemical reagents; when the molecular weight is fairly high, all these qualities give rise to satisfactory operational properties of polymers of this class.

The softening temperatures of polymers, which constitute the upper limits of the region where they can be employed, are related to thermal stability as follows [212]:

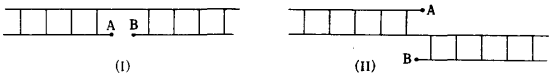
$$T = \frac{\Delta Q}{\Delta S} ,$$

where T is the melting point (or the phase transition temperature), ΔQ the amount of heat absorbed on decomposition of the polymer (or in the transition), and ΔS the entropy of decomposition of the polymer (or the entropy of the transition).

This formula takes into account the following factors: the intermolecular interaction, which determines Q, and the rigidity of the polymer chain responsible for the change in the entropy of the system.

Examination of the thermal stability of polyheteroarylenes of different structures from these standpoints suggested that aromatic polymers with a ladder structure should be more resistant to high temperatures and should be degraded more slowly, since this requires the dissociation of not one but two single bonds [212]. At the same time it was found that despite the differences in structure all the known polyheteroarylenes have similar thermal stabilities, according to dynamic thermogravimetric analysis, which are appreciably lower than suggested. The majority of the polymers begin to decompose in the temperature range 450–500°C with a simultaneous loss of mechanical and other valuable properties (Fig. 1).

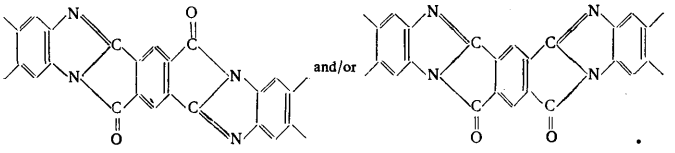
This apparent contradiction between the expected and actual thermal stabilities can evidently be accounted for by the presence of single bonds in the macromolecules, i.e. structural defects in the polymer due to incomplete cyclisation. Analysis of data for the properties of polyheteroarylenes and the study of the process in which they are formed (polyheterocyclisation reactions) showed that it is extremely difficult to attain complete polycyclisation in the polymer macromolecules. This applies particularly to the two-stage synthesis of polyheteroarylenes, in which the cyclisation process takes place in the solid phase, and also to the synthesis of ladder polymers.



In order that the reactive groups A and B should react with formation of a completely cross-linked (ladder) structure, it is necessary that they should be coordinated as in Scheme (I). When Scheme (II) obtains, the formation of a bond requires rotation by 180°, which is extremely difficult for polymers with a high softening temperature owing to the low mobility of the main chain segments. This difficulty increases with increase of the degree of cyclisation.

The study of the polycyclisation kinetics in the solid phase demonstrated differences between the initial and final rates of cyclisation, which is consistent with the entropies of the initial and final stages; the process activation energy does not change appreciably under these conditions [188].

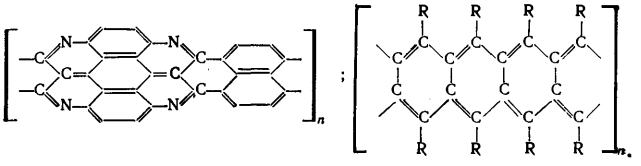
The lower than expected thermal stability of polyheteroarylenes may be caused, apart from the defects in the structure containing non-cyclised sections, by the branching of the polymer, which lowers the packing density and reduces the interchain interaction and also by the configurational and conformational disorder arising in polymer chains owing to the possibility of geometrical isomerism, which also leads to a loss of crystallinity and a decrease of interchain interaction. This can be illustrated using as an example polybenzoylenebenzimidazole obtained from pyromellitic dianhydride and 3,3′-diaminobenzidine, which consists of a mixture of *cis*- and *trans*-isomers (in relation to the benzene ring of pyromellitic acid) [175]:



Among the known polyheteroarylenes, phenylated polyquinoxalines have been attracting special attention; the closure of the quinoxaline ring is apparently favoured so much by thermodynamic and kinetic factors that these polymers are formed extremely readily at room temperature, have high molecular weights, and are fully cyclised, being at the same time fusible and soluble, i.e. capable of being worked [213–215].

A comparative study of the thermo-oxidative degradation of polyphenylquinoxalines and some of the most thermostable polymers—polybenzothiazoles—(under isothermal conditions, since the oxidation processes develop over a period of time) demonstrated a clear advantage of the phenylated polyquinoxalines both over polybenzothiazoles and over unsubstituted polyquinoxalines [215] (Fig. 2). The latter finding confirms the earlier hypothesis that the C–H bonds are very readily activated on heating and are the most susceptible to oxidation, particularly in heterocycles [216].

Such high thermal stability of polyphenylquinoxalines is probably related to the freedom from defects in the polymer chains, which can probably be regarded as the maximum attainable for true linear organic polymers. A further improvement of the thermal characteristics of polymers can be partly achieved by creating more condensed polymeric structures of the type



In this case chain termination at one point cannot cause any appreciable changes in the adjacent regions; under these conditions, there is also a high probability of the destruction of the radicals formed, which increases the resistance of the polyconjugated polymer to thermal oxidation [217–220]. However, the thermal characteristics of condensed polymers of this kind are not markedly improved either; this is probably because, with increase in the complexity of polymer structure, it is increasingly more difficult to attain a high degree of cyclisation and freedom from structural defects.

At the same time the requirements of modern engineering for articles based on thermostable polymers (for example, fibres, fabrics, coatings, plastics, etc.) are increasing continuously. Therefore further heat treatment

of finished articles is being employed to an increasing extent. With the aid of structure-forming processes such as carbonisation and graphitisation, it is possible to increase appreciably the thermal stability and heat resistance of the articles. Consequently, for the formation of satisfactory polycyclic structures, it is very important that the heat-treated cyclopolymers should have a defect-free structure, which makes it possible to avoid undesirable degradative processes [221].

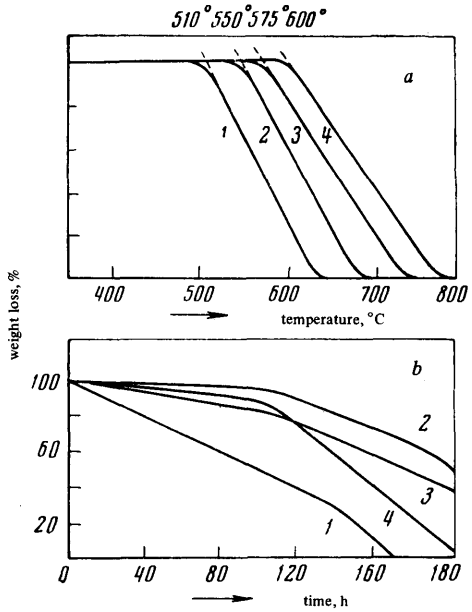


Figure 2. a) Weight loss according to dynamic thermogravimetric analysis in air at a heating rate of 6.67 deg.min^{-1}; particle size 140–240 mesh [1) diether polyquinoxaline; 2) diether polyphenylquinoxaline; 3) polybenzothiazole of type AA–BB; 4) polybenzothiazole of type A–B]; b) weight loss according to isothermal thermogravimetric analysis of the polymers in air at 371°C.

Graphitisation, which involves a more far-reaching heat treatment than carbonisation, leads to materials which should approach, to some extent, carbon structures which also consist of polymers with a very high molecular weight, a two-dimensional and three-dimensional network, and an infinite C/H ratio [218–220].

Thus, depending on the purpose of the final article, an appropriate method should be used for the synthesis of the polymer and for its subsequent heat treatment.

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Institute of Organic Derivatives of the Elements,
USSR Academy of Sciences, Moscow

U.D.C. 615.781

Advances in the Chemistry of Anaesthetics (1961 - 1971)

E.M.Cherkasova, N.T.Pryanishnikova, S.V.Bogatkov, and G.S.Erkomaishvili

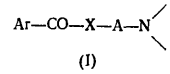
The most important studies on the chemistry of anaesthetics during the last decade are reviewed. Anaesthetics belonging to different classes of organic compounds (aminoalcohol esters, aminoamides, aminoacid amides, aminoketones, etc.) are considered mainly in terms of the relation between structure and physiological activity. Much attention has been devoted to the consideration of the available literature data on the mechanism of the action of anaesthetics.
The bibliography includes 411 references.

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I. INTRODUCTION

During the ten years which have elapsed since the publication of our previous review[1], the total number of reports dealing with anaesthetics† has continued to increase. More than two hundred publications now appear on this subject every year, more than half of which deal with the problems of the mechanism of anaesthetic action, while the syntheses of new preparations are published in brief patent reports with increasing frequency. The result of electrophysiological, physicochemical, biochemical, and other studies discussed below make it possible to formulate fairly definite ideas about the mechanism of the action of anaesthetics with aminoester and amide structures at the cellular and subcellular levels. However, by no means all problems may be regarded as solved. In the first place this applies to the mechanism of the action of anaesthetics at the molecular level and to the determination of the relative role of factors responsible for the quantitative differences in the strength of anaesthetics. The latter problem is closely related to that of the specificity of their action. An enormous amount of experimental data have shown, on the one hand, a high specificity–small changes in structure lead to a sharp decrease in activity up to its complete disappearance[1-9], while at the same time drastic structural changes—for instance, transition from aminoesters to aminoketones or amines involving a complete change in all chemical characteristics—do not deprive the preparation of its capacity to interrupt the nerve pulse. Admittedly, the absence of experimental data makes it impossible to rule out the hypothesis that in such cases the mechanism of action at the cellular or molecular level is different and such substances cannot then be called anaesthetics, although the final physiological result is the same. So far we are forced to treat these substances together with "typical" anaesthetics having ester and amide structures in accordance with the terminology adopted by the authors who describe them. However, considerable difficulties then arise in the classification of published data. Therefore, in the present review the available results are described on the basis of ideas which may be regarded as a development of the old concept of the "anaesthesiophoric group" (I), although its limitation has already been noted[1]:



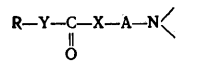
(I)

Statistical data have shown that, despite the wide variety of structures investigated, certain groups are nevertheless encountered most frequently in reactive compounds. These include the amino-group (about 98%) and the carbonyl group (about 80%). Most anaesthetics, including the most active preparations which have found applications, contain both these groups. This suggests that the above combination of functional groups is important for the formation of the steric structure and distribution of electron density in the molecule which is responsible for anaesthetic activity. The environment of these groups, particularly that of the carbonyl group, may be extremely varied and the "structure–activity" problem reduces mainly to the analysis of the nature and mechanism of the influence of substituents in various parts of the molecule on pharmacological activity. There are many views on this topic. Thus, according to Löfgren[10], the strength of anaesthetics is related to the electron density at the oxygen atom of the carbonyl group, which behaves as an electron donor. In many cases, this factor is undoubtedly important—in particular it can account for the increase in the strength of anaesthetic action following the introduction of electron-donating groups (NHR, OR) in the *para*-position of diethylaminoethyl benzoate and the opposite effect of electron-accepting groups such as NO_2. Similar observations have been made for aminoacid amides[11,12] and a number of other types of anaesthetic substances[13] and sometimes it was even possible to observe a quantitative correlation between anaesthetic activity and electron density at the C=O bond[14]. The increase of the activity of the compounds on replacing the ester group by the amide group can itself be related to the increase of electron density at the carbonyl oxygen atom[11].

On the other hand, many facts demonstrate the inadequacy of this hypothesis. Thus when the compounds

†A terminology somewhat different from that current abroad is used nowadays in the Soviet literature; instead of the terms "local anaesthetic" and the Russian equivalent "mestnyi anestetik" employed previously, the term "anaesthetic" is now used, while "narcotic" corresponds to the term "general anaesthetic". This terminology will be used in the present review.

under consideration are represented by the general formula (II)

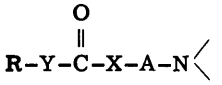


(II)

where X and Y can represent NH, NR, O, S, or C< and A is an alkyne chain or an aromatic residue, it is found that the anaesthetic activity is retained not only on replacement of O by NH but in many cases also on their replacement by the CH_2 group. These groups are isoelectronic and in most cases isosteric, whence one may conclude that geometrical (steric) effects play a considerable role. Numerous data concerning the high activity of compounds containing an *ortho*-disubstituted benzene ring—amino-esters [15-17], anilides [8,9,18,19], and many others—support this view.

Thus, although at present the mechanism of the action of anaesthetics can be regarded as established in broad outline, it is as yet impossible to determine unambiguously the general relation between the structure of the compounds and their anaesthetic activity—different factors are of primary importance in different cases. The "kind" of atoms and their relative positions are probably not the only important (and possibly not the most important) factors; other significant factors are physical parameters characteristic of the molecule as a whole: the relation between hydrophilic and lipophilic properties, the general distribution of the electron cloud, and other features which are related to molecular structure in a complex manner. Recognising this, in classifying anaesthetics we are nevertheless obliged to employ the structural principle as the only one possible at present. It is based on formula (II) and the classification has the form shown in Table 1.

Table 1. Classification of compounds of the type



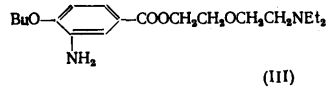
X	Y	Type of compound	X	Y	Type of compound
O	C<	Aminoalcohol esters	C<	NH	Aminoacid amides
NH	C<	Aminoamides	O NH	NH O	Carbamates
C<	O	Aminoacid esters	C<	C<	Aminoketones

II. ANAESTHETIC ACTIVITY OF COMPOUNDS CONTAINING AMINO- AND CARBONYL GROUPS

1. Aminoalcohol esters (X = O, Y = C<)

As before, most attention is devoted to varying the acid component of the molecule in esters of diethylaminoethanol $RCOOCH_2CH_2N(C_2H_5)_2$ and related aminoalcohols. Studies on the classical series of substituted benzoic acids—aminobenzoic [20-23], alkylbenzoic acid [15,24], alkoxybenzoic [16,25-31], and others [32,33]—are being continued. It has been found that the increase of activity in the series *ortho* < *meta*- < *para*-alkoxybenzoic acids [26] and on enlarging R from C_1 to C_4 as well as its decrease when R is branched take place in parallel with the change in the surface activity of these compounds and in many cases (for positional isomers) a parallel variation with partition coefficients is observed.

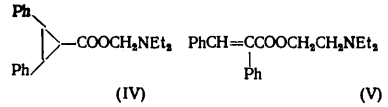
Promising preparations have been found among *p*-alkoxyethoxybenzoates [25] and 2,6-dimethylbenzoates [15]. The latter act over longer periods, possibly owing to steric hindrance to hydrolysis due to the *ortho*-methyl groups, which is characteristic also of other *ortho*-substituents [17]. Among alkoxybenzoic acid derivatives, it was possible to find a substance (III) combining high anaesthetic and vasoconstrictor activities [21]:



(III)

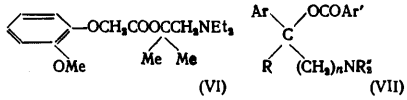
On the other hand, despite their high activity, the aminoesters of halogenobenzoic acids were found as a rule to be unsuitable owing to their considerable toxicity and side effects [29,32].

The esters of certain other aromatic [34-36] and heterocyclic acids [37-42] and also of cinnamic acid and its analogues [43,44] were found to exhibit anaesthetic activity. The derivatives of 2,3-diphenylcyclopropane-1-carboxylic acid [45] may be included among acids of this type. It is interesting to note that the (−)-isomer of (IV), which is a compound in this series, was found to be twice as active as the (+)-isomer. Shah and Ketcham [43] observed that the *trans*-form of compound (V) has a higher anaesthetic activity than the *cis*-isomer:



(IV) (V)

Finally, a high activity has been found in many aminoesters of diarylacetic and similar acids [16,46-51] and also in phenoxyacetates [52-54]. Thus compound (VI), the toxicity of which is smaller by a factor of 7, gives rise to an anaesthetic effect lasting twice as long as that of xylocaine [54]. This confirms the earlier conclusion [1] that the presence of a conjugated chain is not always necessary for anaesthetic activity and that the substituent R in compounds (II) need not necessarily be an aromatic group or its vinylogue:

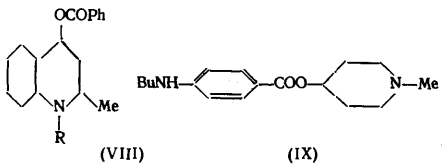


(VI) (VII)

Relatively less attention has been devoted in recent years to varying the alkyl and amino-components of the aminoester molecules. The esters of aliphatic-aromatic aminoalcohols [44,52,53,55-63], including derivatives of type (VII), [52,55-60] were studied in greater detail in this respect. As in many other series, it was found that the shape of the molecule and the dimensions of its constituent units play a significant role in the activity of these compounds [52]. Thus compounds with a trimethylene chain proved to be the most effective, while derivatives of aminoethanols and aminobutanols are relatively inactive [52,56,57]. The accumulation of alkyl substituents round the ester group promotes a high activity, which may be attributed to their electron-donating influence, leading to an increase of electron density at the C=O group and to steric effects,

for example in consequence of the resulting hindrance of hydrolysis. On the other hand, the introduction of various substituents in Ar or Ar′ does not have satisfactory results [52,55,59]. The activity decreases sharply when Ar or Ar′ are replaced by saturated residues [52,58,60,61].

The role of the geometrical structure may be followed by analysing data for the activities of the stereoisomeric esters of γ-piperidinols and γ-decahydroquinolinols [64-68]. It was found that, among benzoates of type (VIII), the esters with a *cis*-diaxial disposition of the CH_3 and C_6H_5COO groups and the *trans*-junction of the rings are much less toxic and more active in terminal [caudal!] and conduction anaesthesia than their epimers. In infiltration anaesthesia the behaviour is somewhat different—here the highest activities are shown by the *trans*-isomers with an equatorial C_6H_5COO group [65,68]. The change from the *trans*- to the *cis*-junction of the rings reduces both activity and toxicity in all cases.



(VIII) (IX)

Similar conclusions were reached by Nobuo [69] in a study of decahydroisoquinoline derivatives. Among piperidine derivatives, the axial isomers show the most effective properties [68,70]. All these data confirm the earlier hypothesis [52] of the importance of the geometrical structure of the molecule in view of the necessity for similarity (isomorphism) of the anaesthetic and a receptor surface for the activity of the preparation.

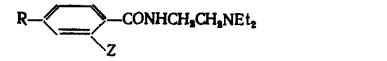
In conclusion we may note a few other aminoesters which exhibit a high anaesthetic activity—"paridocaine" (IX) [23] which has a more prolonged and intense action than novocaine, 2-piperidinoisopropyl diphenylacetate which is 40 times more effective than xylocaine in surface anaesthesia and 3 times more effective in infiltration anaesthesia [71], 2-diethylaminoethoxyethyl benzoate ("kallocaine") which is twice as effective as xylocaine on surface administration and four times as effective on administration by infiltration [72], and also certain other preparations containing ester oxygen in the alkyl chain [73,74].

Other ways of varying the alkyl and amino-components of the aminoester molecules, involving the doubling of the number of functional groups, the introduction of sulphur atoms or the hydroxyamino-group, and the use of various heterocyclic structures, were not appreciably successful [16,27,75-80].

2. Aminoamides (Y = C<, X = NH)

Among aminoamides (i.e. diamines in which one amino-group is acylated), the amides of the heterocyclic acids, which include the familiar anaesthetic sovcaine (cinchocaine, dibucaine, percaine), have been investigated in greater detail [3,5b,81,82]. The activity of these compounds increases as a rule after the introduction of bulky alkyl and alkoxy-groups [81]. It is interesting that the amides of 3-alkoxycinchoninic acid do not exhibit anaesthetic activity, in contrast to the 2-alkoxy-derivatives [39].

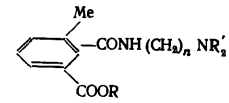
Alkyl and alkoxy-groups promote the appearance of pharmacological activity not only in the series of sovcaine analogues but also among the amides of substituted benzoic acids, which were previously frequently regarded as relatively unpromising [1]. Thus *o*-alkoxybenzamides, particularly the *o*-butoxy- [83,84], *o*-benzyloxy- [85], and *o*-allyloxy-derivatives [86], for example compound (X), proved to be effective, their anaesthetic activity being close to that of xylocaine; 2,4,6-trimethyl- [87,88] and 6-alkoxycarbonyl-2-methylbenzamides (XII) [89] are also active. The activity of the diamide (XI) [90]



(X, Z=OCH2CH=CH2)
(XI, Z=NHCOC6H17)

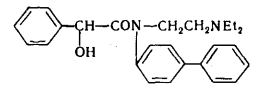
exceeds that of novocaine by a factor of 200.

Compounds containing substituents in the *para*-position are usually less active, but some of them, for example *p*-$ClC_6H_4OCH_2CONHCH_2CH_2NR_2$, are nevertheless used in view of their low toxicity [91].

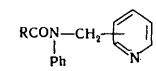


(XII)

A number of studies have been made on aminoamides with an arylated amide group [92,93]; according to the authors, compound (XIII) is a powerful anaesthetic:

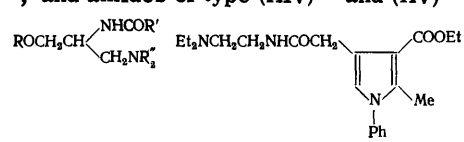


(XIII)



(XIV)

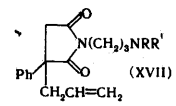
Among other active aminoamides, mention may be made of 4-alkoxyphthalimides [94], 3,3-diphenylacrylamides [95], and amides of type (XIV) [96] and (XV) [97]:



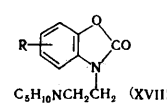
(XV) (XVI)

Compound (XIV), in which the structures of an aminoamide and aminoacid ester are combined, and which is said to induce rapid, stable, and prolonged anaesthesia [98] is interesting. Among dibasic acid imides, which attracted attention recently, compounds (XVII) [99], (XVIII) [100], and a number of others [101,102] proved to be active anaesthetics.

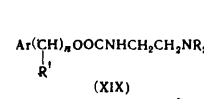
One can also mention the aminoamides of carbamic acids of type (II) (X = NH, Y = O), the infiltration activity of many of which is equal to that of xylocaine. As in other classes of compounds, in the series of substances of type (XIX) the maximum activity is attained with Ar = 2,4-$(CH_3)_2C_6H_3$ and 2,6-$(CH_3)_2C_6H_3$, while *p*-CH_3O, *p*-NH_2, and *p*-Cl substituents reduce it [103]:



(XVII)



(XVIII)



(XIX)

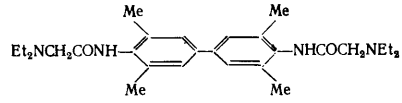
3. Aminoacid imides (X = C<, Y = NH)

Aminoacid amides are a class of compounds to which most attention has been devoted during the last decade. This is due to the abundance of very active preparations

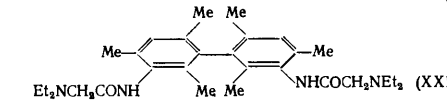
belonging to this class. It is sufficient to mention xylocaine, trimecaine (mesocaine), prilocaine (cytanest) and others. Starting with the structure of xylocaine, detailed studies were made on a wide variety of its analogues[8,9,104]. Studies involving the changes in amide moiety of the molecule, primarily by the introduction of various substituents into the anilide group, have been particularly numerous. As already mentioned, one of the most important factors here are the general lipophilic properties of the molecule, the enhancement of which by the introduction of additional methyl groups (for example in trimecaine[8,9,18]) or by replacing a methyl group by larger substituents[19] leads to an increase of activity; in the last case the fact that the structure of the amide group is sterically hindered may also play an important role.

Numerous compounds containing groups more polar than alkyl substituents in the benzene ring have been investigated. Alkoxy- and aryloxy-derivatives proved to be the most interesting[88,104-108] and, whereas the C_6H_5O group has the most marked effect in the *meta*-position, the $C_6H_5CH_2O$ and $C_6H_5CH_2CH_2O$ groups are most effective in the *para*-position[8,9]. Introduction of the more hydrophilic OH, $OCOCH_3$, and SH groups as well as halogen atoms or the NO_2 group in the benzene ring increases the activity sharply or completely abolishes it[12,88,107,109]. In contrast to other hydrophilic groups, the amino-group has a promoting effect on pharmacological properties, particularly in the 4-position[12,88].

Interesting data were obtained in the study of compounds which may be regarded as "dimeric" analogue of xylocaine (XX) or trimecaine (XXI)[8,9,45]. It was found that, when the distance between the nitrogen atoms in such a structure,



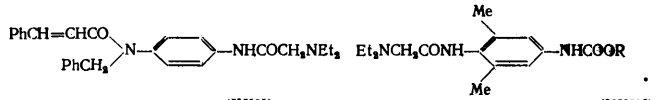
(XX)



(XXI),

is about 10.3 Å, the activity of the preparation is extremely high, when the distance is greater than this it is approximately equal to the activity of the monofunctional compound, and when it is less the activity falls sharply. These results partly indicate the possibility of many-centre addition of the anaesthetic to the receptor.

Certain other combinations of two amide groups in the molecule lead to highly effective anaesthetics, for example in compound (XXII)[110] or (XXIII)[111] whose toxicity is low, the activity of the latter exceeding that of xylocaine by a factor of 10, 20, and 60 respectively for R = C_4H_9, i-C_5H_{11}, and C_6H_{13}:

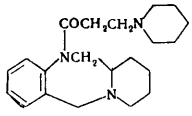


(XXII) (XXIII).

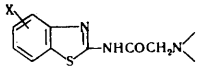
However, in most cases additional carbonyl-containing groups do not improve the properties of aminoacid amides[112-116].

Together with a substituted benzene ring as the aromatic residue, other aromatic and heterocyclic fragments have been frequently introduced into the aminoacid amide molecule. It was found that high activity and its long duration are characteristic of certain aminoacylamide derivatives of naphthalene[117,118] and phenothiazine[50,119-122]. However, the latter frequently exhibit an irritant action on the tissues and for this reason are unsuitable. Unexpectedly the results[120,121] show that, despite the generally held view, certain quaternary salts of 10-aminoacylphenothiazines are not inferior to tertiary amines in their anaesthetic activity or actually superior to them, The author claims that the activity of the preparations depends mainly on the dimensions of the group introduced on quaternisation. Bearing in mind the low activity of the preparations and their considerable irritant action, one might have doubted these claims, but recently a further report has been published[123] in which it is shown that xylocaine methochloride acts like xylocaine itself and the "dose–response" relation is approximately the same for both preparations. Possibly the mechanisms of the action of the base and the quaternary salt are nevertheless different, although so far there are no literature data on this question.

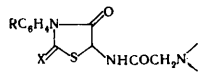
The interesting tricyclic amide (XXIV) has an anaesthetic activity equal to that of xylocaine and its toxicity is low (LD_{50} = 500–1250 mg kg^{-1}),[124]



(XXIV)

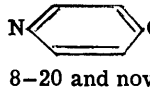


(XXV)

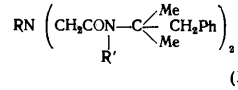


(XXVI).

A number of very active preparations have been discovered by Indian investigators[125-129] and other workers[130-131] among aminoacyl derivatives of thiazoles, benzothiazoles, and thiazolidinones [(XXV)–(XXVI)] and also among the analogous bispiperazine derivatives. The absence of conjugation between the NH–CO group and the aromatic ring in compounds of type (XXVI) is striking. Such conjugation is probably not obligatory, which does not apply only to the above types of compounds—the number of active local anaesthetics discovered in the series of benzylamides[132-137] and compounds with an aromatic terminal group still more remote from the amide moiety has increased in recent years[138-141]. Some of these, for example the bisamides (XXVII), are extremely active[139,140,142]; in particular, the compound with R = $HOCH_2CH_2$ ("oxethazine) and also its analogues with R = $HOCH_2CHC_2H_5$, *p*-$NO_2C_6H_4COOCH_2CH_2$ and



$COOCH_2CH_2$ surpass sovcaine by a factor of 8–20 and novocaine and xylocaine by a factor of 2000 to 4000, while their toxicity is low (for oxethazine, LD_{50} = 400 mg kg^{-1}) and their irritant action is only slight. It is interesting that the activity disappears completely with R = $HO(CH_2)_3$.[140] Thus the position of the benzene ring in a molecule is not always of primary importance:

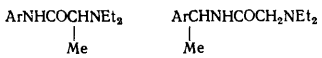


(XXVII).

However, the norbornane and cyclohexane analogues of xylocaine exhibit only an extremely weak anaesthetic effect[143]. These data as well as a number of others described above suggest that the aromatic moieties in the molecule of the anaesthetic are not important solely because of their direct influence on the properties of the carbonyl group. Probably their role is largely to ensure that the compound is soluble in lipids and is capable of

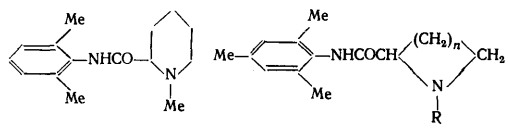
binding to the receptor via non-covalent bonds (hydrophobic binding, π-complex formation, etc.).[11]

Studies[144,145] on the pharmacological properties of *N*-aminoacylephedrines, which are interesting because all eight possible isomers of the amides formed by D- and L-*NN*-dimethylphenylalanines with D- and L-ephedrine and pseudo-ephedrine were investigated and it was shown that derivatives of L-*NN*-dimethylphenylalanine are the most active, merit consideration. On this basis, the authors put forward certain hypotheses concerning the structure of the receptor with which the above substances can interact. It was also shown for compounds (XXVIII) and (XXIX)[146] that the L-isomer has a much higher anaesthetic activity than the D-isomer. Recently this was observed for the anilides of *NN*-dimethylalanine[147]. On the other hand appreciable differences between the activities and toxicities of the D-, L-, and DL-isomers of prilocaine (see below) were not observed[148]:



(XXVIII) (XXIX) .

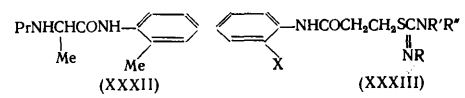
Together with studies on the amide component, much attention has been devoted in recent years to varying the aminoacyl component in aminoacid amides[108,132,135,149-180]. Thus many piperidinoacetamides, particularly those containing several methyl groups in the piperidine ring, proved to be highly active anaesthetics with low toxicity[132-135,149,150]. Together with carbocaine (mepivacaine), which has been known for a long time, its *N*-butyl analogue bupivacaine (marcaine) (XXX), which has a very prolonged anaesthetic action and low toxicity, has been actively investigated recently[151-153]:



(XXX) (XXXI) .

Studies on a series of mesidides of azacycloalkane-α-carboxylic acids (XXXI)[8,9,154-156] showed that, with increase of ring size (n = 2, 3, 4), the surface anaesthetic activity increases and the infiltration activity falls. The activity also increases with increase in the size of the group R, the optimal properties being obtained with R = C_4H_9, i-C_4H_9, and cyclo-C_6H_{11}. As a result of these investigations, two new highly active anaesthetics of type (XXXI) (n = 2)—pyrromecaine (R = C_4H_9) and cyclomecaine (R = cyclo-C_6H_{11})—have been proposed and introduced into clinical practice.

Compounds with other heterocyclic groups (pyrrole, nortropane, morpholine, and piperazine[133,149,157-161] and also with branched or polar aliphatic substituents at the nitrogen atom[162,163] are as a rule relatively inactive or toxic and behave as tissue irritants.



(XXXII) (XXXIII) .

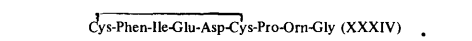
On the other hand, substances with a secondary amino-group, particularly so called prilocaine (propitocaine, cytanest, L 67) (XXXII), continue to attract interest[118,151,164-169]. According to a number of investigators, the activity of prilocaine is equal to that of xylocaine *in vivo*, while the duration of its action is longer and its toxicity lower, although in tests on an isolated neuromuscular preparation it was inferior to xylocaine[168]. The difference is attributed to the lower rate, compared with xylocaine, at which it is washed out by blood, although its *in vivo* decomposition is faster, which accounts for its lower toxicity[168]. Certain *N*-butyl derivatives, for example α-butylamino-3-chloropropionanilide, which according to Malatesta et al.[170] is 79 times more active than xylocaine, are not inferior to prilocaine. Compounds with an NH_2 group are as a rule inactive.

Compounds (XXXIII), which can be classified as aminoacid amides only by convention, have an unusual structure. Some of them [for example, compound (XXXIII) with X = R′ = R″ = H and R = cyclohexyl] are much more active than xylocaine on surface and subcutaneous administration[171,172].

The data on the role of alkylation of the amide nitrogen are contradictory. Thus, according to Kurihara et al.[173], the introduction of an alkyl group into the amide group of xylocaine analogues increases their activity, while the toxicity remains constant. Similar results have been obtained for *N*-benzyl derivatives[174]. On the other hand, according to other workers[132,175], *N*-cyclohexyl and *N*-ethyl derivatives of mesocaine are relatively inactive.

The branching of the aminoacid chain structure appears to have a mainly favourable effect, most probably as a result of an enhancement of lipophilic properties and a change in molecular geometry. This can be seen for the dimethyl analogue of priplocaine (LA - 012) which is superior to xylocaine and prilocaine both as regards activity and duration of action[176], as well as for certain other compounds[177,178]. Many derivatives of β-aminopropionic[179], γ-aminobutyric[106], and β-aminoisobutyric acids[180] are active, although the increase of their activity is frequently accompanied by an increase of their irritant properties and toxicity.

In conclusion mention should be made of the anaesthetic properties of the polypeptide (XXXIV)[181], which can be reasonably considered in this section, since it contains amide bonds:



Unfortunately quantitative data concerning its activity have not been quoted, although it has been stated that it also exhibits a vasoconstrictor activity and that its activity is potentiated by other anaesthetics.

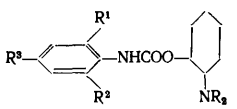
Aminoacid sulphonamides, some of which [for example, $ArNHSO_2CH_2CH_2(C_2H_5)_2$] have anaesthetic properties, can also be probably included in the class of compounds considered here[182].

4. Aminoacid esters (X = C<, Y = O)

In contrast to aminoacid amides, there has been a considerable decrease of interest in aminoacid esters without an amino-group in the alcoholic component. These compounds can be regarded as analogues of aminoalcohol esters with an "inverted" carboxy-group, such structural transformation being apparently unfavourable for pharmacological properties. Among the few substances that have been investigated[183-188], only preparations belonging to the group of aryl esters of *N*-morpholine- and *N*-methylpiperazine-α-carboxylic acids are of interest[183-185]. While their structures are similar to that of xylocaine, their activity is higher for the same toxicitv but they do cause appreciable tissue irritation. The other aminoacid esters investigated recently do not show an appreciable anaesthetic activity.

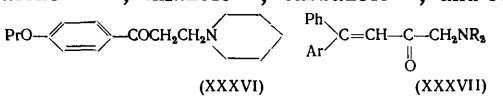
5. Carbamates (X = O, Y = NH)

The Czech school of investigators have been investigating compounds of this class most vigorously [186-193], concentrating attention mainly on 2,6-disubstituted carbanilates. As in many other instances discussed above, it was found that, together with physicochemical properties, the steric influence of *ortho*-constituents plays a significant role, since 2,6-dichloro-, 2,6-dimethyl-, 2-alkoxy-, and 2-aryloxy-derivatives have all been found to be active [103,186-180,194]. Some of them are 5–17 times more active than cocaine in surface anaesthesia and 7–20 times more active than novocaine in administration by infiltration, while having approximately equal toxicities [190]. 2-Butoxy-4,6-dimethylcarbanilate [195], 2-chloro-6-methylcarbanilate [194], and also the carbamates (XXXV) with a somewhat modified ester moiety are extremely active [192,196]. Among them, compound (XXXV) with R′ = CH_3, R^2 = Cl, R^3 = H and R_2N = NC_5H_{10} is 35 times more active than cocaine. Other carbamates with anaesthetic activity which may be mentioned are derivatives of *N*-pyridylcarbamic acids [197,198], phenothiazine-10-carboxylic acid [199], phenothiazine-10-dithiocarboxylic acid [200], and certain carbamoylazepines [201].


(XXXV)

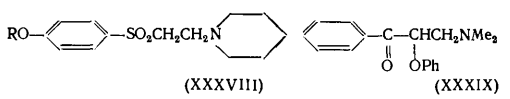
6. Aminoketones (X = C<, Y = C<)

A detailed review of aminoketones with anaesthetic activity was published quite recently [202]. Investigators concentrated attention mainly on the modification of the structure of falicain (XXXVI)—an active anaesthetic discovered at the beginning of the 1950's. It was found that, instead of the benzene ring, it was possible in principle to employ almost any aromatic residue—naphthalene [203,204], thiazole [205], carbazole [206], and others:


(XXXVI) (XXXVII)

The vinylogues of (XXXVII) are several times more active than xylocaine [207,208], in contrast to their hydrogenated analogues [207]. One should mention that, in contrast to falicain, the ketone (XXXVII) is an α-amino-derivative. Certain other α-aminoketones [209-211] and γ-aminoketones [212,213] were found recently to have anaesthetic activity. It was discovered that a sulpho-analogue of falicain—the aminosulphone (XXXVIII)—has a higher anaesthetic activity [214].

Among compounds produced by varying the amino-group, derivatives of hexamethyleneimine proved to be promising in this respect [202,215,216], particularly p-propoxy- and p-butoxy-β-*N*-hexamethyleneiminopropiophenones, the activity of which exceeds that of falicain and dicain, while their toxicity is lower and they do not give rise to side effects. The second preparation has been called "hexacaine"; the *p*-ethoxy-derivative ("ethamine") is somewhat less active [202].


(XXXVIII) (XXXIX)

A further increase in ring size is undesirable—derivatives of heptamethyleneimine are completely inactive [217]. The best results are obtained by the introduction of propyl [218] and butyl [219] substituents in the 4-position of the piperidine ring; substituents in the 2- and 3-positions are less effective [218]. Compounds with acyclic nitrogen are as a rule relatively inactive, although the activity increases sharply after the introduction of the phenyl [220] or phenoxy-group [16] in the α-position—for example, compound (XXXIX) is three times more active than cocaine in surface anaesthesia and five times more active than novocaine in infiltration anaesthesia [16].

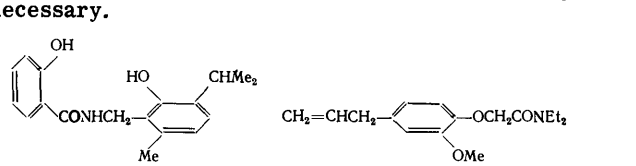
Compounds containing a carbonyl group attached directly to the heterocycle, which in this case combines the function of the amino-group and the carbon skeleton, may be classified as aminoketones with a structure somewhat different from that of falicain. Among these substances, 3-acylpiperidines [221] and 4-acyldecahydroisoquinolines [222] proved to be anaesthetics. Attempts to enhance the anaesthetic effect by doubling the aminoketone structure were unsuccessful—the aminoketones obtained by the Mannich reaction from diacetylbenzene are much less active than the corresponding monoaminoketones [223].

III. ANAESTHETIC ACTIVITY OF COMPOUNDS CONTAINING ONE FUNCTIONAL GROUP

Although the majority of active anaesthetics contain both amino- and carbonyl groups, nevertheless many studies dealing with compounds containing only one of these functional groups have been published.

1. Amides

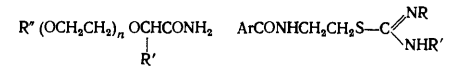
The amides of acids without a second amino-group have been known for a fairly long time as anaesthetics. Usually anaesthetic activity is observed either in acylated anilines [224,225] or in aromatic acid amides [226,227]. As in many other instances, the general lipophilic properties of the molecule and the steric environment of the amide group play a significant role here. Thus among amides of the type $CH_3(CH_2)nCONHAr$, compounds with n = 5–7 are the most active, while derivatives of lower acids are inactive [225]. Among aromatic acid amides, *o*-substituted derivatives are the most active, for example salicylamides of type (XL) [226]. However, the contiguity of the aromatic ring and of the amide group is not obligatory—many other derivatives show anaesthetic activity, including the amides of phenoxyacetic acid, among which an interesting preparation "detrovel" (XLI) has been discovered. It causes rapid anaesthesia, the intensity of which is equal to that induced by dicain but the duration of its action is much shorter [228], which is frequently necessary.


(XL) (XLI)

In subsequent investigations it was shown that the anaesthetic activity disappears when the acetamide moiety is eliminated from compound (XLI) or when an ethylene

group is introduced. The degree of anaesthesia diminishes sharply also after various modifications of the acetamide moiety, after the displacement of methoxy- and allyl groups to other positions in the aromatic ring, or after replacing the allyl group by the ethoxycarbonyl group [229,230].

Among other amides, anaesthetic activity has been found in *N*-acylated derivatives of heterocycles [231,232] and in certain derivatives containing a ring carbonyl group [233-235]. Readily water soluble polyglycol ethers of type (XLII) containing an amide group have also been patented as anaesthetics [236]:



(XLII) (XLIII)

2. Amidines and Derivatives of Guanidine, Isothiuronium, etc.

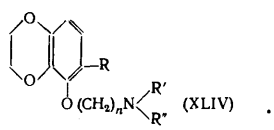
Earlier, it was noted [1] that compounds containing amidine, guanidine, and similar groups possess anaesthetic activity. Active amidines [88,237] and guanidines [238,239] have also been synthesised in recent years. Isothiuronium derivatives, anilides [171,172], and benzamides (XLIII) [240,241] are likewise powerful anaesthetics. Certain isothiuronium derivatives have an activity exceeding that of xylocaine by a factor of 4-20 in surface administration and by a factor of 2-6 in administration by infiltration. Regan et al. [241], who compared this structure with 2-aminothiazoles which also exhibit anaesthetic activity, assert that the $-S-C\begin{matrix}N-\\ \diagdown\\ N-\end{matrix}$ group can be regarded as a new anaesthesiophoric structure.

Finally, there exists yet another group, resembling the carbonyl group and related to it genetically, namely the aldoxime group, which also gives rise in many cases to anaesthetic activity in compounds containing it [242,243]. It has been noted [242] that, together with the aldoximes $ArCH{=}NOCH_2CH_2NR_2$, the isomeric *N*-oxides are active.

3. Amines

Despite the fact that anaesthetics employed in midical practice have not been found as yet among simple amines, these substances are apparently of interest by virtue of a number of advantages—relative simplicity of synthesis and resistance to hydrolysis-which are in many instances combined with high anaesthetic activity.

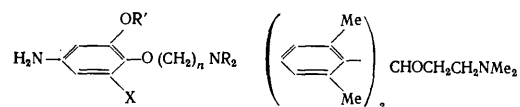
Compounds containing an ether oxygen atom (or several such atoms) together with the amino-group are most widely used. Thus Daukshas and coworkers made a detailed study of benzodioxan derivatives (XLIV) [244-246]:



(XLIV)

They showed that, in order to exhibit anaesthetic activity, compounds of this type must contain hydrocarbon substituents with a specified "bulk". The introduction of additional polar groups (OH, NR'_2) destroys their activity, apparently as a result of the enhancement of the hydrophilic properties, since the activity may be restored by the removal of the polar dioxan ring. The preparation with $n = 2$, $R = CH_2CH{=}CH_2$, $R' = H$, and $R'' = CH_3$ ("benzodiocaine") the activity of which exceeds that of dicain by a factor of 2.2 in terminal [caudal?] anaesthesia, while its toxicity is smaller by a factor of 2, proved to be the most active.

Anaesthetic properties have also been found in a series of phenyl [247-258], benzyl [259], and diphenylmethyl ethers [260-263], particularly those with *ortho*-substituents. It may be that the oxygen atom in these compounds simulates in some way the carbonyl group, which gives rise to similar structural characteristics. Thus it has been found that the activity, toxicity, and irritant properties of the series of compounds (XLV) become more marked with increase in the size of the group R', while substitution of a hydrogen atom in amino-group by an acyl group lowers both their activity and toxicity [250,251]. Basic ethers with a polyoxyethylene chain, $R(OCH_2CH_2)nNR'_2$, where R = 2-guaiacyl or 2-thyminyl residue ($n = 2-4$) [254], the analogous diphenylmethyl ethers [260], and also the diphenylmethyl ether (XLVI), which is 10 times more active than novocaine but causes irreversible tissue changes [261], were found to be active. Phenyl ethers substituted in the *meta*- and para-positions exhibit anaesthetic properties much more rarely [255,256].

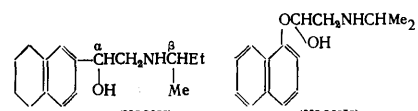


(XLV) (XLVI)

It is important to note that amines, aminoethers, and analogous compounds, which do not have an "anaesthesiophoric" structure, as a rule exhibit another kind of pharmacological activity (spasmolytic, antihistamine, cholinolytic, etc. [257,262,264-282]), as well as anaesthetic activity, which may be regarded as evidence in support of the non-specific mode of their action. Some of the most active (according to the data of the investigators who described them) amines, are listed in Table 2. Judging from the wide variety of structures of these preparations, the position of the oxygen atom in the molecule is not too significant and its role probably reduces to imparting to the substance the required physicochemical properties.

The mechanism of the anaesthetic activity of aminoalcohols is still obscure. Presumably the hydroxy-group of these compounds influences mainly their lipophilic properties. However, one cannot rule out the possibility that certain aminoalcohols do not act directly in the organism but are initially rapidly oxidised to the corresponding aminoketones, which then exhibit anaesthetic properties. Evidence in support of this hypothesis is provided by the finding that anaesthetic activity is as a rule shown by secondary aminoalcohols containing the group ArCHOH, which can be readily oxidised to ArC=O; for example, the tetrahydronaphthalene derivative (XLVII) has an anaesthetic effect comparable to that of xylocaine and novocaine [283,284].

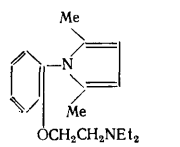
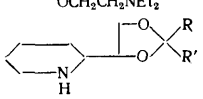
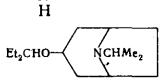
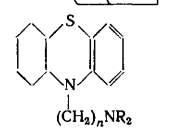
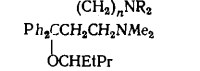
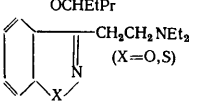
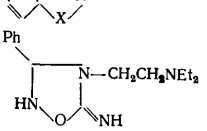
It is interesting that among the four stereoisomers (XLVII), which have been called "butydrine", the αSβS-isomer shows the highest anaesthetic activity, while the αRβR- and αRβS-isomers exhibit a β-blocking activity [284]:



(XLVII) (XLVIII)

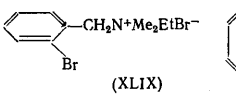
Certain other aminoalcohols of this type are also active as anaesthetics[207,285-288]; on the other hand, active preparations with a hydroxyl remote from the aromatic rings are fairly common[288-295], in particular propranolol (XLVIII) the activity of which is close to that of xylocaine[294,295].

Table 2. Physiological activity of certain oxygen-containing amines.

Compound	Anaesthetic activity	Other types of activity	Refs.
	3 times and 20 times higher than the activities of cocaine and novocaine respectively	Antagonist of pilocarpine, morphine, and $BaCl_2$; 30 times more effective than papaverine	257
	50-80 times higher than the activity of novocaine	Spasmolytic	265
	100 time higher than the activity of cocaine	Antihistamine and atropinemimetic	266
	2-10 times higher than the activity of cocaine	Spasmolytic, sedative, antihistamine, analgesic, etc.	268-270
	Lower by a factor of 1.5 than the activity of dicaine	Cough suppressant midriatic	271
	Exceeds the activity of xylocaine	Spasmolytic, antihistamine	272
	3 times and 5 times higher than the activities of cocaine and novocaine respectively	Vasodilator, analgesic	273,274

The activity of certain phenolic compounds[296,297] and also of aminoalcohols of the diphenylmethanol series[298], which are altogether incapable of being converted into carbonyl compounds, have likewise been mentioned. Therefore the role of the OH group as well as that of the C–O–C bond in the anaesthetic activity of amines remains obscure, particularly since amines without other functional groups have shown such activity in fairly numerous instances.

Thus 2-naphthylalkylamines, which exhibit pronounced surface-anaesthetic properties, for example $Ar(CH_2)_nN(CH_3)C_5H_{11}$ (Ar = β-naphthyl), are more active than novocaine by a factor of 16.[299] The relations discovered between the physiological properties of these compounds and their structures are approximately the same in surface and conduction anaesthesia and are close to those observed in other series of compounds. β-(4-Methyl piperidinoethyl)naphthalene is 13 times as active as cocaine (in 0.5% solution)[300]. Anaesthetic properties have been found also in cyclohexylphenylamines[301], in bretilium (ornid) (XLIX)[302], although this compound does not in fact contain a quaternary nitrogen atom, in the diamine (L) which is 20 times as active as xylocaine and 4 times as active as dicain[303], in α-amino-4-dimethylaminodiphenylmethane, which gives rise to prolonged and intense anaesthesia[304], in many aromatic[305-310] and heterocyclic amines[311-322], and also in certain saturated amines[323,324]. However, all these compounds are as a rule non-specific and exhibit several types of physiological activity.



(XLIX) (L)

4. Compounds without Nitrogen Atoms

The anaesthetic activity of alcohols, particularly that of benzyl alcohol, has been known for a long time. The activities of more complex alcohols[325] and their derivatives, in particular of polyethers of the type $C_nH_{2n+1}(OCH_2CH_2)_mOH$ (Zipf and Dittmann[326]), and many others[327] have been mentioned in a number of studies. It was found that the anaesthetic activity of these compounds increases in parallel with chain length and with enhancement of their lipophilic properties and increase of the partition coefficient. It was discovered that the anaesthetic activity of the ether $(C_6H_{13}OCH_2OCH_2CH_2)_2O$ ("efiran") is close to that of cocaine, but the compound is less toxic and does not have an irritant action[328]. The alkyl esters of *p*-hydroxybenzoic[329] and gallic[330] acids were found to be active, the anaesthetic effect increasing with the size of the alkyl group; for example, the activity of dodecyl *p*-hydroxybenzoate is 6 times as great as that of novocaine[329]. However, the available data are too fragmentary to reach any conclusions concerning the mechanism of the action of compounds of this type.

IV. SOME HYPOTHESES ABOUT THE MECHANISM OF THE ACTION OF ANAESTHETICS

Until recently ideas about the mechanism of the action of anaesthetics were extremely speculative and indefinite and were based exclusively on empirical relations between structure and activity and therefore could hardly be regarded as of general validity. Direct electrophysiological investigation of the action of anaesthetics as substances acting on the generation and transmission of nerve excitation became possible only as a result of advances in the study of the generation and transmission of the nerve pulse in the last decades. Furthermore, detailed physicochemical and biochemical studies on anaesthetics were made in recent years.

As shown above, substances with a wide variety of structures and consequently differing in reactivity exhibit anaesthetic properties. All these findings suggested that the physicochemical processes determined by the physicochemical properties of the anaesthetics play an important role in the mechanism of anaesthetic action. For blocking action to take place, the anaesthetic must initially penetrate to the reaction site and must then interact with the receptor. At least three factors are therefore important for anaesthetic activity: (1) the capacity of anaesthetics to pass through various biological membranes (not linked directly to the nerve tissue) to the nerve fibres and to be adsorbed on their surface; (2) the capacity of anaesthetics to penetrate the membrane of the nerve fibre and their behaviour in the excited membrane; (3) the interaction

of anaesthetics with specific (in the chemical sense) receptor structures. The mechanism of the action of anaesthetics can be usefully considered on these lines.

Almost all anaesthetics are organic bases and therefore their capacity for ionisation is important for their activity. It was believed for a long time that the unionised base is in fact responsible for the anaesthetic effect. This conclusion was readily confirmed by well known data according to which the minimal effective blocking concentration of anaesthetics decreases with increase of the pH of the medium [331-334]. However, it was shown comparatively recently that there is no direct relation between basicity and anaesthetic activity [8,335] and, since with the majority of active preparations in the region of physiological pH values the concentration of the cation is more constant than that of the base, it was concluded that the cation is the active form of the anaesthetic [335-340]. On the other hand, it is evident that anaesthetics penetrate the myelin sheath of the nerve fibre [336-338] or the axon membrane [341] in the uncharged form. In a study of the effect of two lidocaine derivatives (pK_a = 6.3 and 9.8) on the membrane of the squid axon at different pH it was shown that the anaesthetics penetrate the membrane in the uncharged form but block the action potential only in the form of the cation [341]. The majority of anaesthetics employed in practice have pK_a = 7.0 to 9.0. [8,335,340] This limitation also suggests that both forms of the anaesthetic are important for its action: the unionised base is responsible for the migration of the anaesthetic to the reaction site and its cationic form is responsible for the direct interaction between the anaesthetic and the receptor [337,339,341-343].

For the anaesthetic substance to be able to reach the site of its activity (the axon membrane) it must have a definite solubility in water and lipids. The earlier attempt to relate the anaesthetic activity of substances to their partition coefficients between aqueous and lipid phases were unsuccessful [10,11]. However, recently it was possible to observe such a relation [8,344]. On the other hand, it has been discovered that the anaesthetic and surface-active properties of anaesthetics vary in parallel [345-347]. The surface and interfacial activities of compounds, their capacity to penetrate liquid monolayers and at the same time their anaesthetic activity increase when the pH of the medium is raised from 3.5 to 7.35. [335,348] It has been shown that anaesthetics are not only adsorbed by phospholipid layers but are also capable of interacting with certain phospholipids in cell membranes via ion–ion and ion–dipole mechanisms forming a 1 : 2 complex like Ca^{2+} ions [349]. They are probably bound to the phosphate groups of the lipids which interact with Ca^{2+} ions [349,350].

Thus, by virtue of their lipophilic properties and surface activity, anaesthetics penetrate the neural membrane and alter its physicochemical properties: hydrophobic properties [351], electrical resistance [352] and pH, while at high concentrations they coagulate aqueous phospholipid dispersions. The change in physicochemical properties alters the functions of the membrane, which is reflected in physiological processes. The parallel variation of the physicochemical properties (lipophilic properties, partition coefficient in the nerve, capacity for adsorption in the nerve, surface and interfacial activities, and capacity for adsorption) and of anaesthetic activity mentioned above is related to these factors, which has made it possible to explain certain empirical relations between the structure of the compounds and their pharmacological activity and even to predict the activity of many new preparations [8,335].

Clearly no serious investigation is now conceivable without taking into account the influence of the physicochemical factors discussed above. The action of anaesthetics is nowadays treated mainly on the basis of the generally accepted theory of the generation and propagation of electric potentials in neuromuscular tissue [353,354].

Experimental studies have shown that anaesthetics interfere with the transmission of the nerve pulse, mainly by their capacity to inhibit the increase of permeability to sodium in the region of the Ranvier node in the axon membrane [355-364].

There are divergent opinions in the literature concerning the specific action of anaesthetics on the sodium system of the membrane. The majority of investigators believe that anaesthetics reduce the "maximum permeability to sodium", i.e. block the sodium channels in the membrane [355,357,360,365-369]. On the other hand, there are data [370,371] showing that anaesthetics can activate the systems governing the permeability of the membrane to sodium. This is supported by the known ability of anaesthetics to "interfere" with the motion not only of Na^+ but also of other ions: potassium [359,360,372,373], calcium [360-362,371,374-378], lithium [363,379], nickel, cobalt, cadmium [380], and magnesium [381]. In this respect the study of the effect of Ca^{2+} ions, to which much importance is attached in the mechanism of the change in the ionic permeability of the membrane on excitation [354,381-383], is of particular interest.

The most common view held at present is that Ca^{2+} ions and anaesthetics act at the same sites in the membrane and therefore compete for the sodium "pores" or "transferring agents" in the conducting system of the membranes [351,361,270,383-386]. Such sites are probably the phosphate groups of lipids [349] acting as agents transferring Na^+ and K^+ ions across the membrane.

The charged molecules of anaesthetics can strongly inhibit this process by combining with the anionic centres of phospholipids [349,375]. However, the hypothesis of a direct competitive interaction of anaesthetics and Ca^{2+} is not free from contradictions [349,371,385].

There are numerous data indicating the capacity of anaesthetics to react not only with phospholipids, the role of which in the mechanism of the action of anaesthetics has been proved, but also with other natural substances—thiamine [387], RNA [388], adenine, and ATP. [389] It has been shown that anaesthetics are antagonistic to various amino-acids and alkaloids [390,391], nucleotides [389,392,393], and proteins [386,394,395], which has led to the hypothesis that such interactions are in fact responsible for anaesthetic activity [6,396]. One of the most thoroughly developed hypotheses of this kind is that of the competitive antagonism of anaesthetics and acetylcholine in their interaction with a specific receptor [397-400]. Such antagonism has indeed been demonstrated in a number of experiments [401-403]. However, despite a number of attempts, the result of numerous investigations on different lines contradict the acetylcholine theory of the generation and transmission of the nerve pulse in the peripheral nerve [396,404,405].

Theories which explain the action of anaesthetics by their influence on cell metabolism should also probably be treated with much caution. This explanation is unlikely primarily because even the fastest of the enzymatic processes involving the decomposition or synthesis of lipids known at present take place at a rate the order of magnitude of which is much lower than that of the blocking of ion transport, which constitutes the basis of the generation and transmission of the nerve pulse. Next it was shown that neural conduction and its blocking by

anaesthetics can be achieved equally in the presence of natural axoplasm and after its replacement by an artificial salt solution[406]. Hence one may conclude that a specific effect of anaesthetics develops in the membrane and does not depend significantly on intracellular oxidation-reduction processes. Therefore, despite the numerous data showing the influence of anaesthetics on cell respiration[407-409] and its coupling with phosphorylation[410], there are no grounds for the belief that these processes are responsible for specific anaesthetic action, since many anaesthetics are central nervous system depressants and their effect on the oxidation-reduction processes in the nerve tissue can be in no way fully related to the observations made on the axon membrane. So far it is difficult to assess the role of enzymes in the effect of anaesthetics on the Na^+ and K^+ transport systems, since hitherto it has not been established exactly what types of enzymes may be included in the operation of the sodium-potassium pump in the membrane[411]. Moreover, so far there have been no quantitative estimations of the reactivity of anaesthetics in their interaction with the structures of the excited membrane (receptor), of the kind that have been made, for example, for cholinesterases, MAO [monoaminooxidase] inhibitors, cycloserine derivatives, and other substances. It appears that due consideration has yet to be given to this important problem.

Summarising the above findings, the action of anaesthetics can be represented as follows. By virtue of their surface-active and lipophilic properties, anaesthetics pass through various media to the axon, are adsorbed on the cell surface in concentrations sufficient for their activity, and penetrate the excited axon membrane in the region of the Ranvier node, altering at the same time the orientation of the molecules in the membrane. The permeability to anaesthetics is greatly influenced by the degree of their ionisation and their capacity to exist in the region of physiological pH as an equilibrium mixture of two forms—the cation and unionised base—is important for their anaesthetic action, since their activity depends on both these species. In the axon membrane anaesthetics are held by virtue of the interaction of the cation with the polar group of phospholipids and phosphoproteins and as a result of the hydrophobic interaction of the unionised base. In the course of binding to the axon membrane, anaesthetics most probably enter into a competitive interaction with Ca^{2+} ions, which play an important role in the mechanism of ion transport. The displacement of Ca^{2+} from the structure of the membrane is one of the main causes of the marked inactivation of the sodium transport system with a simultaneous retention or even some increase of the rest potential. As a result of these effects, in the presence of anaesthetics and the normal transmembrane potential difference and the normal content of bivalent ions in the medium are no longer sufficient to maintain the membrane in a state of readiness for response to stimulation. Therefore, in order to restore this capacity, it is necessary to either increase considerably the above potential difference by a hyperpolarising current or to increase the concentration of Ca^{2+} (or Ni^{2+}) in solution. Only at very high concentrations of the anaesthetic are the hyperpolarising current and Ca^{2+} or Ni^{2+} ions no longer capable of restoring fully the damaged structure of the membrane. Thus anaesthetics inactivate the mechanism of the change in permeability to sodium on depolarisation. In consequence of all the phenomena enumerated above, electrical activity ceases without depolarisation. This probably constitutes the essential feature of the action of anaesthetics.

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Lomonosov Moscow Institute of Fine Chemical Engineering

Institute of Pharmacology and Chemotherapy, Academy of Medical Sciences of the USSR

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Super-pure Materials from Metal-organic Compounds

B.G.Gribov

Work on the preparation of super-pure materials by the decomposition of metal-organic compounds is reviewed. The decomposition methods, and the factors which influence the purity of the elements and compounds obtained, are discussed. The possible applications and the advantages of the thermal decomposition method are pointed out. 69 references.

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I. INTRODUCTION

The preparation of super-pure materials by using metal-organic compounds (MOC) has been intensively studied in recent years. In principle, the method is based on the decomposition of metal-organic compounds to elements or compounds whose purity is determined (depending on the experimental conditions) by the purity of the initial metal-organic compound.

The purification of substances such as metals, which are involatile and refractory by virtue of their atomic crystal lattice, has to be carried out at high temperatures and is therefore liable to cause contamination of the product by the material of the apparatus. On the other hand, the thermal decomposition of MOC (leading to the formation of elements or compounds) can be carried out at relatively low temperatures, with negligible contamination of the product by the material of the apparatus. Substances produced by thermal decomposition of MOC can be obtained either in the form of powders or as coatings on substrates of practically any composition and configuration.

Contamination with carbon is always a possibility in the preparation of pure substances by thermal decomposition of MOC, and therefore the use of volatile inorganic hydrides is preferred for the preparation of super-pure elements such as boron, germanium, phosphorus, tin, arsenic, antimony, etc.[1] However, volatile inorganic hydrides are known for only a few of the elements, and therefore the method has only a limited application. On the other hand, metal-organic compounds are known for practically all the elements; they can be synthesised by selective methods which already remove a number of impurities, and they can be intensively purified by fractional distillation, chromatography, or crystallisation. Furthermore, the carbon contamination of the product can be reduced (often to negligible proportions) by proper control of the thermal decomposition reaction and by suitable choice of the initial MOC.

In addition to their application in the preparation of highly pure substances by thermal decomposition, MOC are often used and purified on their own account. Organic derivatives of metals are very useful for the extraction of small amounts of one element from large amounts of

another element in order to concentrate the minor component or to purify the major component.

The aim of the present review is to collate the existing fund of experimental data on the preparation of pure substances from metal-organic compounds. We shall discuss the behaviour of trace impurities during the synthesis and purification of the MOC, and we shall analyse the effect of experimental conditions and of the type of MOC on the carbon contamination of the resulting elements and compounds. We shall stress the wide range of possible applications of the method, and the prospects of obtaining superpure substances from metal-organic compounds.

The review is confined to papers in which the purity of the initial metal-organic compounds and of the resulting elements and compounds is stated.

II. SELECTIVITY OF THE METHOD OF SYNTHESIS OF METAL-ORGANIC COMPOUNDS, AND PURIFICATION

In order to produce high-purity substances by thermal decomposition of metal-organic compounds we must have access to extremely pure MOC. The freedom of the resulting metals, alloys, and compounds from trace impurities of other elements is determined by the amount of these impurities present in the original metal-organic compound. Modern techniques of organic chemistry allow us to prepare metal-organic compounds of practically every element, and even to vary the type of compound produced from any one element, so that the scope of physicochemical methods of purification becomes much wider than in the corresponding inorganic systems. The most convenient and most widely used methods of purification of MOC are fractional distillation, chromatography, recrystallisation, and extraction. Zone melting, sublimation, molecular distillation, and other special methods can be used in particular cases.

One of the most important aspects of the preparation of super-pure substances by the decomposition of MOC is the tendency of the methods of synthesis to exclude originally present impurities. This is a consequence of the selectivity of the usual methods of synthesis. Thus, the preparation of alkyl derivatives of non-transition metals can be expected to yield a product in which the concentration of transition-metal impurities is lower than in the initial reagents, since transition metals do not readily form alkyl derivatives. A similar type of purification occurs also during the synthesis of organic transition-metal compounds, which tend to be purified from non-transition metal impurities.

Gribov and coworkers [2] have studied the behaviour of trace elements during the synthesis of non-transition MOC for the special case of the preparation of trimethylgallium from methyl iodide and a gallium-magnesium alloy:

$$Ga + Mg + CH_3I \rightarrow (CH_3)_3Ga + MgI_2$$

and other workers have reported similar studies of the preparation of the etherate of trimethylgallium by the Grignard reaction [3]

$$CH_3MgI + GaCl_3 \xrightarrow{(C_2H_5)_2O} (CH_3)_3Ga \cdot O(C_2H_5)_2,$$

and of bis-ethylbenzenechromium by Fischer's method [4].

The impurities in the initial gallium, chromium, and aluminium chlorides were probably present as chlorides and oxide chlorides, those in the metallic magnesium and aluminium were probably present as elements. Under the conditions used for the synthesis of these metal-organic compounds, impurities in the initial reagents could find their way into the final product as methyl, chloromethyl, oxide chloride, and arene compounds.

Table 2. Impurity content of bis-ethylbenzenechromium and of the starting reagents.

Substance	Impurity content, wt.%						
	Al	Mg	Mn	Si	Ni	Fe	Ti
$CrCl_3$	$>1\cdot10^{-2}$	$1\cdot10^{-2}$	$7\cdot10^{-3}$	$2\cdot10^{-2}$	$2\cdot10^{-3}$	$2\cdot10^{-3}$	$6\cdot10^{-3}$
$AlCl_3$	—	$1\cdot10^{-2}$	$3\cdot10^{-4}$	—	$4\cdot10^{-5}$	$>1\cdot10^{-2}$	$1\cdot10^{-3}$
Al	—	$>1\cdot10^{-2}$	$5\cdot10^{-3}$	—	$5\cdot10^{-3}$	$1\cdot10^{-2}$	$1\cdot10^{-2}$
$(EtC_6H_5)_2Cr$	$<1\cdot10^{-4}$	$3\cdot10^{-4}$	$3\cdot10^{-4}$	$<1\cdot10^{-3}$	$<1\cdot10^{-3}$	$<1\cdot10^{-3}$	$<1\cdot10^{-3}$

Analytical results for trace impurities in the initial reagents and in the final products (trimethylgallium etherate, trimethylgallium, and bis-ethylbenzene chromium) are summarised in Tables 1 and 2. It is evident that the impurity content is much lower in the MOC than in the starting materials. For example, the concentration of aluminium, magnesium, and silicon (which do not form the corresponding bis-arene compounds) is 1–2 orders of magnitude lower in bis-ethylbenzenechromium than in the starting materials. Trimethylgallium etherate and trimethylgallium contain 10–100 times less copper, magnesium, titanium, zinc, iron, nickel, aluminium, manganese, silver and silicon than the reagents used in their preparation (magnesium and gallium trichloride).

Table 1. Impurity content of trimethylgallium etherate, trimethylgallium, and starting reagents*.

Substance	Impurity content, wt.%												
	Cu	Mg	Zn	Al	Ti	Si	Sn	Pb	Cr	Mn	Fe	Ni	Ag
Mg tech.	$\geqslant5\cdot10^{-3}$	—	$>4\cdot10^{-2}$	$>1\cdot10^{-2}$	$1\cdot10^{-3}$	—	$1\cdot10^{-3}$	$>1\cdot10^{-2}$	$2\cdot10^{-3}$	$>5\cdot10^{-3}$	$1\cdot10^{-2}$	$2\cdot10^{-3}$	$5\cdot10^{-5}$
$GaCl_3$ tech.	$3\cdot10^{-4}$	$5\cdot10^{-4}$	$1\cdot10^{-3}$	$>1\cdot10^{-3}$	$1\cdot10^{-3}$	$6\cdot10^{-3}$	$1\cdot10^{-3}$	$>1\cdot10^{-3}$	$1\cdot10^{-3}$	$1\cdot10^{-4}$	$\geqslant1\cdot10^{-3}$	$5\cdot10^{-4}$	$5\cdot10^{-4}$
$(CH_3)_3Ga\cdot O(C_2H_5)_2$	$5\cdot10^{-5}$	$6\cdot10^{-5}$	$4\cdot10^{-4}$	$2\cdot10^{-4}$	$<1\cdot10^{-4}$	$2\cdot10^{-4}$	$4\cdot10^{-4}$	$4\cdot10^{-3}$	$<1\cdot10^{-3}$	$<1\cdot10^{-4}$	$4\cdot10^{-4}$	$1\cdot10^{-4}$	$<3\cdot10^{-5}$
Ga tech.	$3\cdot10^{-4}$	$1\cdot10^{-4}$	$2\cdot10^{-3}$	$1\cdot10^{-4}$	$<3\cdot10^{-3}$	$6\cdot10^{-3}$	$1\cdot10^{-4}$	$4\cdot10^{-3}$	$2\cdot10^{-3}$	$<5\cdot10^{-4}$	$6\cdot10^{-3}$	$5\cdot10^{-4}$	$4\cdot10^{-4}$
$(CH_3)_3Ga$ **	$6\cdot10^{-5}$	$5\cdot10^{-5}$	$2\cdot10^{-4}$	$1\cdot10^{-4}$	$<1\cdot10^{-4}$	$2\cdot10^{-4}$	$9\cdot10^{-5}$	$3\cdot10^{-4}$	$<4\cdot10^{-6}$	$2\cdot10^{-6}$	$9\cdot10^{-5}$	$5\cdot10^{-5}$	$<3\cdot10^{-6}$

*The tabulated values are the average of 3–5 determinations.

**Technical magnesium was used to prepare this material.

Trimethylgallium and its etherate are most effectively purified from those trace elements which do not form alkyl derivatives, and whose chlorides have a volatility very different from that of the gallium MOC. Even when the elements present as impurities in the starting materials can form the corresponding metal-organic compounds (zinc, tin, silicon) their concentration is significantly lower in the final MOC.

The behaviour of trace impurities in gallium chloride during the synthesis of gallium MOC has been studied by a radioactive tracer method[2] for the particular case of zinc. The isotope ^{65}Zn was added to gallium trichloride as zinc chloride, and the gallium trichloride was used to prepare trimethylgallium etherate. Only a very small fraction of the zinc present in the gallium trichloride was detected in the final trimethylgallium etherate: most of the radioactivity remained in the still residue left after distillation of the main product.

The selectivity of the methods of preparation of aluminium, tantalum, and niobium alkoxides has been fully discussed[5,6]. Aluminium alkoxides were prepared by treating metallic aluminium with the appropriate alcohol, and the alkoxides of tantalum and niobium by treating the chlorides of the metals with alcohols.

Analysis for trace impurities in the starting materials and in the final products showed a decrease in concentration by 1–2 orders of magnitude. This purification is due both to the selectivity of the method of synthesis and to the efficiency of the separation during distillation of the alkoxides, resulting from the large difference in volatility between the main product and the impurities. The total concentration of trace impurities (Ag, Ti, Fe, Pb, Mn) in the Ta and Nb alkoxides was 1×10^{-4} wt.%.

Existing data on the behaviour of trace impurities during the synthesis of various types of MOC indicate not only that transition metals are separated from non-transition metals (and *vice-versa*), but also that the concentration of all trace elements in the final product is very substantially decreased. We can therefore conclude that the methods used to prepare MOC have a high selectivity.

The reactions used in the preparation of metal carbonyls, widely applied in the production of super-pure metals, have a specially high selectivity. With an iron ore containing a large amount of impurities as the raw material, the synthesis of iron carbonyl almost completely eliminates[7] impurities such as S, P, Mn, As, and Cu. The resulting iron carbonyl contains other metal carbonyls as the only impurity. For example, the concentration of nickel in iron pentacarbonyl is $\sim 1 \times 10^{-2}$%. The vapour pressure of nickel tetracarbonyl is appreciably higher than that of iron pentacarbonyl, which allows the nickel content to be decreased to 1×10^{-4}–2×10^{-4}% by bubbling an inert gas through the iron pentacarbonyl at 40–60° and finally redistilling the product[7].

Umilin and Tsinovoi[8] have described some interesting observations on the removal of organic impurities during the synthesis of MOC. Tetrabutyltin was prepared from stannic chloride and a butyl magnesium halide. The butyl bromide was analysed chromatographically, and found to contain various homologues and isomers (1 mole.% of combined s- and t-butyl bromides, 7×10^{-2}% of n- and isopropyl bromides, 4.0×10^{-2}% of ethyl bromide). These impurities react with magnesium to form the appropriate alkyl magnesium bromides, which then react with stannic chloride to give compounds of the general formula $R'_nSnR''_{4-n}$, where R′ and R″ are s-Bu, t-Bu, n-Pr, i-Pr, and Et. Chromatographic analysis of the resulting tetrabutyltin showed that the total amount of organotin compounds containing the isobutyl radical, the propyl radical, and the ethyl radical had been reduced to $\sim 1 \times 10^{-1}$, $\sim 5.3 \times 10^{-5}$, and 3.3×10^{-4}% respectively. These results indicate a purification from organic impurities by 1–2 orders of magnitude during the synthesis of tetrabutyltin.

The purity of the MOC used to prepare super-pure materials must be of the highest order. When the MOC is thermally decomposed any trace impurities of other elements are transferred almost quantitatively to the final metal or compound, whether produced as a powder or as a coating. Therefore the purity of the ultimate product is largely determined by the concentration of trace elements in the original MOC. Purity of the initial MOC is vitally important in the preparation of semiconductor compounds ($A^{II}B^{IV}$, $A^{III}B^{V}$, etc.). The need for extreme purity is particularly evident in the preparation of semiconductor compounds (gallium arsenide) in the form of epitaxially grown layers[9,10]. In addition to traces of other elements, the MOC may contain organic impurities such as the initial reagents or solvents used in their synthesis. These impurities are less harmful than traces of other elements to the electro-physical properties of the resulting materials. However, the contamination of super-pure materials produced by the decomposition of MOC with carbon, resulting from deep-seated chemical changes in the organic compounds, is determined mainly by the type and the structure of the MOC and by the conditions under which these compounds are thermally decomposed. These problems are discussed in detail in Section III.

Another aspect of the MOC purity problem is the "individuality" of the compound, i.e. the presence or absence of homologues of the organic compound or of any other derivative of the metal. The presence of impurities in the form of homologues is determined by the type of MOC and by the method of synthesis used. Thus, metal alkyls produced by the Grignard reaction are, effectively, individual compounds, free from other organic derivatives of the same metal, if the starting reagents are sufficiently pure. The same is not true of alkyl-substituted bis-arene compounds of the transition metals[11–14]: for example, alkyl-substituted bis-benzenechromium is always obtained as a mixture of homologues, due to transalkylation of the alkyl-substituted aromatic hydrocarbons in the presence of the aluminium chloride added to the reaction mixture. Thus, the synthesis of bis-ethylbenzenechromium yields[13,14] a mixture of mono-, di-, and trisubstituted homologues of bis-benzenechromium, as well as a series of asymmetric products such as benzene-ethylbenzenechromium. The concentration of homologues in the mixture is determined by the experimental conditions, varying from fractions of one percent to tens of percent. The preparation of chromium coatings from these complex mixtures is not an easy process: the MOC vapour from the evaporator is led into the reactor, where it flows over the objects to be coated, which are held at a temperature higher than the decomposition temperature of the organochromium compound. The MOC decomposes on the hot surface, and a chromium film is formed. However, since the various organochromium compounds present in the mixture have different boiling points and vapour pressures, and also different decomposition temperatures, it is difficult to maintain a constant concentration of chromium MOC vapour in the reactor, and therefore the rate of deposition and the electro-physical parameters (such as resistivity) of the

film are not easily controlled. Hence, it is necessary to separate the bis-arene compounds of transition metals into their individual compounds before attempting to prepare metallic coatings by the thermal decomposition of these materials.

Table 3. Organic impurities in bis-ethylbenzenechromium, and sensitivity of the gas–liquid chromatography method of analysis used.

Impurity	Impurity content, mol.%	Analytical sensitivity, mol.%
Benzene	1.0	$1.2 \cdot 10^{-2}$
Toluene	$1.0 \cdot 10^{-2}$	$1.0 \cdot 10^{-2}$
Ethylbenzene	1.8	$6.0 \cdot 10^{-3}$
o-Ethyltoluene	$1.0 \cdot 10^{-2}$	$1.0 \cdot 10^{-2}$
o-Diethylbenzene	1.0	$5.1 \cdot 10^{-3}$
Triethylbenzene	$5.0 \cdot 10^{-1}$	$7.2 \cdot 10^{-3}$
bis-Benzenechromium	$5.0 \cdot 10^{-2}$	$6.0 \cdot 10^{-3}$
bis-Toluenechromium	$4.0 \cdot 10^{-2}$	$4.0 \cdot 10^{-2}$
Benzene-ethylbenzenechromium	12.2	$1.9 \cdot 10^{-2}$
bis-Ethylbenzenechromium	66.5	—
Ethylbenzene-*o*-diethylbenzenechromium	15.7	$3.0 \cdot 10^{-2}$
bis-Diethylbenzenechromium	1.5	$5.1 \cdot 10^{-2}$
bis-Triethylbenzenechromium	$6.0 \cdot 10^{-2}$	$6.0 \cdot 10^{-2}$

The most detailed studies of the preparation of bis-arene compounds of the transition metals in a high state of purity have been made on bis-ethylbenzenechromium [13,14]. The results of a gas-chromatographic analysis of one sample of this material are summarised in Table 3.

Benzene-ethylbenzenechromium, bis-ethylbenzenechromium, and ethylbenzene-*o*-diethylbenzenechromium with an impurity content of 6×10^{-2}% have been isolated by fractional distillation of bisethylbenzenechromium.

Bis-arene compounds of chromium can be purified by recrystallisation as well as by fractional distillation. The methyl homologues of bis-benzenechromium in an oxidised form (e.g. as iodides) are crystalline compounds having different solubilities in water, and hence it is possible to prepare alkyl-substituted derivatives of bis-benzenechromium in a relatively high state of purity [5].

Intensive purification of MOC from traces of other elements can be achieved by distillation, fractionation, preparative chromatography, recrystallisation, ion exchange, or extraction. A particularly successful method [15] of extraction of small amounts of one element in the presence of large amounts of another element, whether in order to concentrate the impurity or to purify the major constituent, depends on the formation of inner complexes of the elements. An exchange reaction occurs during the extraction, and as a result the element E′ present in the aqueous phase displaces the element E″ present in the complex. These exchange reactions offer a high selectivity, since the elements which displace E″ are those which are most readily extracted.

Separation of impurities by extraction can be realised in two ways: either by extracting the impurity or by extracting the major constituent and leaving the impurity in the aqueous layer.

Pure cobalt has been prepared [15,16] by the following procedure: an aqueous solution of a cobalt salt is treated with a solution of a cobalt soap (fatty acid salt) in an organic solvent. Impurities whose soaps are more stable than that of cobalt displace cobalt by ion exchange and are transferred to the organic layer. Cobalt solutions containing only traces of iron and copper, and $2–5 \times 10^{-3}$ g litre^{-1} of nickel, have been prepared by this method.

Tetraethoxysilane has been purified from traces of copper, nickel, cobalt, iron, manganese, and other impurities by a complex-adsorption method [17], in which the starting material is treated with sodium diethyldithiocarbamate, which complexes a large number of metals, and the resulting chelates are removed (together with the excess of reagent) by sorption on activated charcoal. Hydrolysis of the tetraethoxysilane purified in this way, followed by heating the resulting silica gel at 650–750°, has yielded samples of silicon dioxide containing aluminium, iron, copper, lead, and other impurities at the $10^{-5}–10^{-6}$ wt.% level.

Clearly, only some of the impurities can be removed from the main element by exchange–extraction methods. Elements whose extraction properties are inferior to those of the main element cannot displace the latter from its compound in the organic phase, and they remain in the aqueous layer.

A more effective method, capable in principle of removing almost any impurity from the aqueous solution has been described by Zolotov and Spivakov [15]. It consists of two main steps. In the first step the main element is extracted in such a way that the whole of the reagent is used up (the excess of the main element need not be very large). All the elements which are extracted less strongly than the main element remain in the aqueous layer. The main element is then re-extracted with an aqueous solution of appropriate acidity, and the pH of the aqueous extract is adjusted to the value used for the initial extraction. The remaining impurities are then extracted (step 2) with the same reagent but in much smaller amount, so that the main element is present in large excess over the reagent. This operation removes the trace elements which can displace the main element from the complex. Practically all metal impurities in zinc chloride and indium nitrate have been removed by this method.

Some examples of the preparation of super-pure metal-organic compounds by different methods are listed in Table 4.

III. METHODS OF DECOMPOSITION OF METAL-ORGANIC COMPOUNDS AND PURITY OF THE PRODUCT

The preparation of pure substances from MOC is based on the ability of these compounds to yield pure metals or compounds under the influence of various forms of energy. The most widely used and better understood methods rely on the decomposition of MOC in the vapour phase by heat, by an electron beam, by the radiation from optical quantum generators, by a gas-discharge plasma, and also by hydrolytic methods in solution.

Depending on the chosen method of decomposition, and on the experimental conditions, the pure substances can be obtained as powders, films (amorphous or polycrystalline), or as single crystals.

The following types of MOC have been used to prepare high-purity materials: metal alkyls and aryls; alkoxides, acetylacetonates, and organic salts; carbonyls, arenes, and some other compounds.

Whereas the purity of the ultimate product in terms of traces of other elements is determined by the purity of the MOC, the problem of contamination by carbon is more complicated and depends on a number of factors.

The general use of MOC for the preparation of pure metals, oxides, and particularly semiconductors was originally thought to be unlikely because of the presence of organic side-products and of the consequent danger of contamination of the final product by carbon and hydrogen.

Table 4. Purity of metal-organic compounds purified by different methods.

MOC	Method of purification	Impurity content, wt.%	Reference
1	2	3	4
$(C_6H_6)_2Cr$	As prepared	Al $2{,}6\cdot10^{-4}$, Cd $2{,}2\cdot10^{-4}$ Cu $3{,}1\cdot10^{-3}$, Fe $2{,}7\cdot10^{-2}$, Mg $1{,}1\cdot10^{-3}$, Mo $1{,}4\cdot10^{-3}$, Si $4{,}1\cdot10^{-3}$	18
$(C_6H_6)_2Cr$	Recrystallised	Al $2{,}6\cdot10^{-4}$, Cd $<2{,}2\cdot10^{-4}$, Cu $1{,}0\cdot10^{-3}$, Fe $2{,}7\cdot10^{-3}$, Mg $4{,}6\cdot10^{-4}$, Mo $1{,}4\cdot10^{-3}$	18
$(C_6H_6)_2Cr$	Recrystallised and sublimed	Cd $2{,}2\cdot10^{-4}$, Cu $1\cdot10^{-3}$, Fe $9\cdot10^{-4}$	18
$(C_6H_6)_2Cr$	Reduction of bis-benzene-chromium iodide	Cu $<5\cdot10^{-5}$, Ti $<1\cdot10^{-3}$, Ni $<1\cdot10^{-3}$, Co $<2\cdot10^{-3}$, Mg $1\cdot10^{-4}$, Mn $<1\cdot10^{-4}$, Al $2\cdot10^{-4}$	5
$(EtC_6H_5)_2Cr$	Distillation	Organic impurities $\leq 6\times10^{-2}$	13, 14
$C_6H_6CrC_6H_5Et$	ditto	ditto	13, 14
$EtC_6H_5CrC_6H_4(C_2H_5)_2$	,,	,,	13, 14
$(EtC_6H_5)_2Cr$	Distillation	Al $<1\cdot10^{-4}$, Mg $3\cdot10^{-4}$, Mn $3\cdot10^{-4}$, Si $<1\cdot10^{-3}$, Ni $<1\cdot10^{-3}$, Fe $<1\cdot10^{-3}$, Ti $<1\cdot10^{-3}$	2
$(C_6H_6)_2CrI$	Crystallisation	Cu $<5\cdot10^{-5}$, Ti $<1\cdot10^{-3}$, Ni $<1\cdot10^{-4}$, Co $<2\cdot10^{-3}$, Mg $7\cdot10^{-4}$, Mn $<1\cdot10^{-4}$, Al $8\cdot10^{-4}$	5
$(C_6H_6)_2CrBr$	ditto	Cu $2\cdot10^{-4}$, Ti $<1\cdot10^{-3}$, Ni $6\cdot10^{-4}$, Co $<2\cdot10^{-3}$, Mg $4\cdot10^{-3}$, Mn $<1\cdot10^{-4}$, Al $6\cdot10^{-3}$, Fe $<2\cdot10^{-4}$	5
$(CH_3C_6H_5)_2CrI$	,,	Cn $4\cdot10^{-5}$, Ti $<1\cdot10^{-4}$, Ni $5\cdot10^{-4}$, Mg $4\cdot10^{-4}$, Mn $9\cdot10^{-5}$, Al $4\cdot10^{-4}$, Fe $1\cdot10^{-3}$	5
$[(CH_3)_3C_6H_3]_2CrI$	,,	Cu $2\cdot10^{-3}$, Ti $<2\cdot10^{-3}$, Ni $2\cdot10^{-3}$, Mg $1\cdot10^{-3}$, Mn $<5\cdot10^{-4}$, Al $6\cdot10^{-4}$, Fe $7\cdot10^{-4}$	5
$(CH_3)_3Ga$		Cu $6\cdot10^{-5}$, Mg $5\cdot10^{-5}$, Zn $2\cdot10^{-4}$, Al $1\cdot10^{-4}$, Ti $1\cdot10^{-4}$, Si $2\cdot10^{-4}$, Sb $9\cdot10^{-5}$, Pb $3\cdot10^{-4}$, Cr $<4\cdot10^{-6}$, Mn $2\cdot10^{-6}$, Fe $9\cdot10^{-5}$, Ni $5\cdot10^{-5}$, Ag $<3\cdot10^{-6}$	2
$(CH_3)_3GaO(C_2H_5)_2$	ditto	Cu $5\cdot10^{-5}$, Mg $6\cdot10^{-5}$, Zn $4\cdot10^{-4}$, Al $2\cdot10^{-4}$, Ti $<1\cdot10^{-4}$, Si $2\cdot10^{-4}$, Sn $4\cdot10^{-4}$, Pb $4\cdot10^{-3}$, Cr $<4\cdot10^{-6}$, Mn $<2\cdot10^{-6}$, Fe $4\cdot10^{-4}$, Ni $1\cdot10^{-4}$, Ag $<3\cdot10^{-6}$	2,19
$(C_4H_9)_4Sn$	Distillation	Organic impurities $<5\times10^{-4}$	8
$Si(OC_2H_5)_4$	Extraction and absorption	Al $3—8\cdot10^{-6}$, Fe $2\cdot10^{-6}$, Mg $2—8\cdot10^{-6}$, Mn $1\cdot10^{-6}—3\cdot10^{-7}$, Cu $2\cdot10^{-6}—8\cdot10^{-7}$, Pb $5\cdot10^{-6}$, B $\sim2\cdot10^{-6}$	17
$Al(O\text{-}i\text{-}C_3H_7)_3$	Distillation	Cu $7\cdot10^{-5}$, Mg $4\cdot10^{-4}$, Ag $4\cdot10^{-4}$, Ti $<3\cdot10^{-4}$, Fe $5\cdot10^{-4}$, Pb $<1\cdot10^{-4}$, Mn $<2\cdot10^{-5}$	5,6
$Ta(OC_2H_5)_5$	ditto		5,6
$Nb(OC_2H_5)_5$	,,	Ag $<1\cdot10^{-5}$, Fe $3\cdot10^{-4}$, Pb $<2\cdot10^{-3}$, Mn $<2\cdot10^{-4}$	5,6

This may be the reason why no attempt was made for many years to prepare semiconductor materials from MOC: only very recently has the successful use of metal-organic compounds in the preparation of semiconductor materials such as epitaxially grown $A^{II}B^{VI}$ and $A^{III}B^{V}$ structures been reported.

A number of approaches which may help to minimise or even to eliminate the risk of carbon contamination may be found in the large fund of experimental information on the decomposition of metal-organic compounds. This belief is confirmed by the many recent reports of the preparation of ultra-high purity materials from MOC. There are two ways of controlling the residual carbon content of materials prepared from MOC. The first relies on the correct choice of MOC and on appropriate control of the decomposition conditions. The second relies on special treatment of the final products obtained from the MOC.

The criteria which determine the best type of MOC structure are the mechanism of thermal decomposition and the likelihood of carbon contamination of the final product.

The decomposition reactions of MOC can be described by the following mechanisms:

1) radical $R_nE \rightarrow n\dot{R} + E$,
2) hydride or olefin $(RCH_2CH_2)_nE \rightarrow nRCH{=}CH_2 + E + H_2$,
3) molecular $L_nE \rightarrow nL + E$.

The first two types of decomposition are typical of alkyl, aryl, and cyclopentadienyl compounds, the third is typical of MOC formed by molecules containing an even number of π-electrons. The most important among the latter are arene and carbonyl compounds of the transition metals, in which the ligands are aromatic hydrocarbons or carbon monoxide.

Side reactions involving the organic radicals and molecules formed during the decomposition of the MOC may lead to contamination of the resulting metal with carbon. Among the most important secondary reactions of the radicals formed by thermal dissociation of MOC, which may influence the purity of the metal produced, are the decomposition of an organic radical to an olefin and hydrogen, or decomposition with C–C bond breaking. Both these reactions have been detected in a study [20,21] of the thermolysis of MOC of tin, germanium, and aluminium. The conclusion of this study was that the lower alkyl radicals tend to decompose by splitting a C–C bond, the higher radicals by splitting a C–H bond.

The influence of the alkyl radical on the purity of the product of MOC decomposition is clearly shown by the behaviour of aluminium-organic compounds [21]. Thus, whereas the pyrolysis of trimethylaluminium is a method of preparation of aluminium carbide, high-purity aluminium containing $\sim 1\times10^{-2}\%$ of carbon can be prepared by thermal decomposition of tri-isobutylaluminium. A similar behaviour is observed also in the thermal decomposition of organogallium compounds: whereas the decomposition of trimethylgallium is accompanied [22] by the formation of a polymeric product of composition $(CH_3Ga)_n$, high-purity gallium metal is obtained from the decomposition of tri-isobutylgallium [5].

Thus, to prepare pure metals by thermal decomposition of MOC we must choose compounds in which the E–R bond energy is small, and the side-reactions of the organic constituents of the molecule occur preferentially by β–C–H (rather than β–C–C) cleavage.

MOC which decompose by the molecular mechanism are suitable for the preparation of pure metals in the form of powders or in the form of coatings. These include bis-arene, arenecarbonyl, carbonyl, and some other organic compounds of the transition metals. The influence of the starting MOC on the carbon and hydrogen content of chromium and molybdenum films prepared pyrolytically has been carefully studied [23–25]. The study included a

series of bis-arene compounds of chromium and molybdenum, the iodides of the bis-arene derivatives of chromium, and some arenetricarbonyl compounds of both metals. The resulting metal films were found to be contaminated by carbon, hydrogen, and (in the case of chromium) oxygen. The chromium films contained between 0.5 and 10% of carbon. The carbon content increased from the arene π-complexes to the arenetricarbonyl compounds of chromium, and within the chromium arene series it increased with the number of alkyl substituents in the aromatic nucleus of the π-complex. The lowest carbon content was found in the chromium films prepared by the pyrolysis of the iodides of bisarenechromium compounds.

Molybdenum films prepared by thermal decomposition of bis-arene and arenetricarbonyl compounds of molybdenum contain more carbon than chromium films prepared under similar conditions from analogous compounds.

Oxygen analysis of the chromium and molybdenum films gave some interesting results. Thus, whereas the pyrolytic chromium films contained 8% of oxygen as Cr_2O_3, the molybdenum films prepared by pyrolysis of bisarenemolybdenum complexes under similar conditions contained no oxygen. The most likely explanation is that both chromium and molybdenum are readily oxidised in the presence of a trace of oxygen, but whereas the chromium oxide is involatile and resistant to reduction by the products of partial decomposition of the MOC, the molybdenum oxide is more volatile, and can be reduced to the metal at temperatures as low as 360–700°.

Evidently, the presence of carbides and oxides in the pyrolytic chromium films can explain their enhanced hardness, mechanical strength, and resistance to acids (as compared with chromium films prepared electrochemically or by vacuum deposition).

It is clear from these results that the purity of metals prepared by thermal decomposition of MOC is largely determined, as far as carbon contamination is concerned, by the type of compound used, and that this contamination can be partly or completely eliminated by suitable choice of the starting compound.

However, the experimental conditions under which the MOC is thermally decomposed are also a very important factor in determining the purity (and in particular the freedom from carbon) of the resulting metals and compounds. Among the most important practical conditions are factors such as the medium, the decomposition temperature, the total pressure in the reactor, the rate of removal of the decomposition products, and the possibility of catalytic reactions.

The temperature at which thermal decomposition is carried out has a profound effect on the decomposition mechanism of the MOC, on the direction and extent of side-reactions, and hence on the purity of the final product.

Work on the bis-arene compounds of chromium and molybdenum has shown that the carbon content of the metal film increases with the temperature at which the MOC is decomposed. Thus, if bis-ethylbenzenechromium is pyrolysed at temperatures in the range 450–700° the carbon content of the chromium films increases from 0.7 to 6%,[23] and in the decomposition of mesitylenetricarbonylmolybdenum it increases from 6 to 10% as the temperature is increased from 400 to 550°.[25]

The higher carbon content is the result of more deep-seated chemical changes in the aromatic hydrocarbons, leading to the formation of free carbon and metal carbides. It is important to note that the aromatic ligands in arene compounds of the transition metals suffer more drastic decomposition than the corresponding aromatic hydrocarbons. Thus, hydrogen evolution is hundreds of times more abundant during the decomposition of bis-benzenechromium than during the decomposition of benzene at the same temperature[18].

A thermodynamic analysis of the decomposition of bis-benzenechromium[26] has shown that reactions leading to the formation of chromium, chromium carbides, and free carbon have a higher probability than reactions in which the only solid products are chromium and carbon. The higher the temperature, the greater is their probability. Hence, the decomposition temperature chosen for the bis-benzenechromium should be as low as possible in order to minimise the carbon content of the chromium films.

An increase in the temperature at which metal-organic compounds are thermally decomposed does not invariably produce an increase in the carbon content of the film: the type of MOC, and the nature of the decomposition products, determine the effect of an increase in temperature. This phenomenon is clearly illustrated by the preparation of pure metals through the pyrolysis of metal carbonyls[27–29]. The decomposition of molybdenum hexacarbonyl by the reaction $Mo(CO)_6 \rightarrow Mo + 6CO$ is accompanied by the side-reaction $2CO \rightleftharpoons C + CO_2$, which is responsible for the contamination of the molybdenum with carbon. On raising the temperature, the equilibrium of the carbon monoxide decomposition reaction is shifted towards the left, and the amount of free carbon decreases. Several workers[27–29] have found that molybdenum coatings prepared by thermal decomposition of molybdenum hexacarbonyl at relatively high temperatures have a lower carbon content.

It follows that a knowledge of the decomposition mechanism of the MOC, and of the side-reactions, is an essential prerequisite to the correct choice of decomposition temperature for the preparation of pure, carbon-free metals. The decomposition temperature can be lowered very significantly by introducing various additives into the reactor: this is an interesting method of decreasing the probability of contamination of a metal or compound prepared by thermal decomposition of MOC. The effect of additives can be explained as follows. An additive can react with the starting reagent, or it can catalyse its decomposition, thus lowering the decomposition temperature of the MOC. It can also react with the decomposition products of the MOC, thus lowering the probability of the side-reactions and raising the purity of the product. Lastly, the additive may deactivate the excited metal atoms formed by the thermal decomposition of the MOC, and modify the crystallisation conditions. Thus, the addition of amines during the thermal decomposition of tetra-alkylgermanium compounds has been shown[30] to favour the growth of monocrystalline germanium "whiskers".

The decomposition temperature of bis-arenechromium compounds can be lowered by using halogen and sulphur compounds as catalytic additives[31,32].

In the thermal decomposition of tetraethoxysilane, the presence of oxygen lowers the temperature of formation of silicon dioxide by ~300°. The catalytic effect of transition-metal salts can give rise to autocatalysis in the decomposition of some MOC. Thus, a chromium halide is formed by disproportionation during the preparation of chromium coatings from halogen derivatives of bis-arenechromium compounds[23,33]; this halide catalyses the thermal decomposition, lowering the formation

temperature of the chromium film and at the same time decreasing its carbon content.

The pressure, and the rate of removal of by-products, have a major influence on the quality and the structure of deposits prepared by thermal decomposition[34]. The pyrolysis of MOC gives rise to gaseous products whose vapour pressure is much higher than the vapour pressure of the original MOC. As a result, the total pressure in the system increases, and the concentration of MOC close to the substrate surface decreases: both these effects tend to lower the rate of deposition. This rate-limitation by pressure is observed at constant rate of removal of the reaction products. If the rate of removal is zero (closed reaction vessel) there is a gradual decrease in deposition rate due to the increase in pressure in the system. If the rate of removal of the decomposition products tends to infinity the rate of growth of the deposit becomes independent of pressure, and is limited by the rate of mass transfer to the substrate or by the rate of the decomposition reaction of the MOC. In all intermediate cases the rate of deposition is pressure-dependent to a greater or lesser extent. The presence of decomposition products near the substrate surface, and the increase in total pressure, tend to favour the adsorption of the decomposition products on the solid deposit and to hinder their desorption, thus increasing the danger of contamination. These observations lead to the following practical conclusion: in the thermal decomposition of MOC, faster depositions and purer deposits are obtained by working at low pressures and by ensuring that the decomposition products are removed rapidly.

Domrachev and coworkers[34] studied the carbon content of molybdenum films as a function of the ratio of the rate of supply of molybdenum carbonyl to the rate of removal of the reaction products, and they found that the carbon content changes from 4.6 to 1×10^{-1} wt.% as the rate of removal is increased from 0.5 to 14.2 litre s^{-1} (surface temperature 602°, $P = 0.1$ mmHg).

Other factors are also known to affect the purity of metals and compounds prepared by thermal decomposition of MOC. For example, the effect of an electric field on the growth of deposits during the thermal decomposition of molybdenum carbonyl has been investigated[38]. It has been shown that the electrostatic field increases the rate of deposition of the metal, drastically lowers the carbon content (to $\sim 1 \times 10^{-2}$%), and lowers the optimum deposition temperature of high-quality films.

In addition to the thermal decomposition method, the hydrolytic method is widely used for the preparation of high-purity materials from MOC in the vapour phase. The method lends itself to the preparation of very pure oxides, mixed oxides, and compounds such as barium titanate. Hydrolysis can be induced by treating the MOC with water vapour, in solutions, or in the vapour phase. Hydrolysis in solutions occurs at room temperature, and the resulting oxides are practically free from carbon. The greatest danger of carbon contamination arises during hydrolysis in the vapour phase. The purity of silicon dioxide prepared by vapour-phase hydrolysis of tetraethoxysilane is profoundly affected by the ratio $Si(OC_2H_5)_4 : \alpha H_2O$, the optimum value of α being a function of the hydrolysis temperature[37]. Thus, the optimum values of α at 427, 727, and 1227° are 2.85, 4.85, and 6 respectively. As the temperature increases, and as α decreases, the amount of carbon incorporated in the solid deposit increases. Whereas powdered silica prepared at 350° and with $\alpha < 3$ is strongly contaminated with carbon (and black in colour), a fine white powder is obtained at the same temperature with $\alpha > 4$. No carbon is detected in the latter sample by i.r. or u.v. spectroscopy.

Thus, the carbon content of materials prepared by the decomposition of MOC can be lowered by a number of methods, including the choice of the best type of starting material and proper control of the experimental conditions. In addition, the carbon content can also be decreased by special treatment of the final product of thermal decomposition. Hydrogen (and, in particular, moist hydrogen) is a very effective medium for the post-treatment of metals such as chromium, molybdenum, tungsten, iron, nickel, and ruthenium. Thus, whereas molybdenum prepared by the pyrolysis of molybdenum carbonyl contains ~1% of carbon, a hydrogen treatment after pyrolysis lowers the carbon content to 1×10^{-2}.[38] Thermal decomposition of iron carbonyl followed by heat treatment of the resulting carbonyl iron in hydrogen yields the purest of all iron powders[7]. The heat treatment of the carbonyl iron removes nitrogen and oxygen impurities as well as carbon. The main impurities in iron powder prepared by thermal decomposition of iron carbonyl are cementite (Fe_3C), the nitride Fe_4N, and magnetite (Fe_3O_4).[7] These impurities react with hydrogen to give metallic iron and gaseous products (water, methane and ammonia). The impurity hardest to remove is elemental carbon, which begins to react with hydrogen at an appreciable rate only above 400°. The purest iron powder is obtained by treating the carbonyl iron powder in a hydrogen atmosphere at the lowest possible temperatures (in the range 300–400°) in a large excess of hydrogen and with continuous removal of the reaction products[7]. The level of purity attainable in iron powder prepared by thermal decomposition of iron carbonyl followed by heat treatment in a hydrogen atmosphere is indicated in Table 5.

IV. PREPARATION OF PURE ELEMENTS, OXIDES, AND OTHER COMPOUNDS

Elements can be prepared in a high state of purity from MOC by methods such as thermal decomposition in the vapour phase or in solutions, photolysis, and electrolysis. The ultimate freedom from trace impurities is determined by the purity of the initial MOC rather than by the method of decomposition. Contamination of the final product by carbon depends mainly, as discussed in Section III, on the type of MOC and on the decomposition conditions.

The advantages of using MOC for the preparation of pure materials are most clearly seen when the ultrapure material is required in the form of a thin coating, or when an alloy of prescribed composition is deposited as a thin film. Alloy films deposited by conventional methods do not always have the same composition as the starting material, because of differences in the evaporation temperature of the alloy components. By choosing MOC of different metals having similar physicochemical properties, or by adding controlled amounts of MOC vapours to the reactor, coatings having the desired component ratio can be deposited by thermal decomposition even on items of complicated shape.

The relatively low decomposition temperature of MOC, and the absence of other reagents or solvents, ensure that metals prepared from MOC are purer than metal prepared by other methods. Chromium prepared by the

pyrolysis of bis-benzenechromium[18] contains fewer trace impurities than electrolytic chromium. The purity of iron prepared by thermal decomposition of iron pentacarbonyl is outstandingly high[7,39].

Because of the selectivity of the methods of synthesis, and of the high purity of the resulting metals, MOC have been used on an industrial scale to prepare specially pure materials. The carbonyl process for the preparation of pure iron[7] is very widely used in industry. It can be described by the following scheme:

$$Fe_{(impure)} + 5\,CO \xrightarrow[P=100-200\ atm]{180-220^\circ} Fe(CO)_5 \xrightarrow{230-330^\circ} Fe_{(pure)} + 5\,CO\,.$$

In the first step of the process the carbon monoxide reacts selectively with an iron-containing ore to give iron pentacarbonyl: this results in considerable purification from traces of other metals. In the second step, pure iron is produced by thermal decomposition and the carbon monoxide is re-cycled.

Table 5. Summary of preparation of pure substances from metal-organic compounds.

Element or compound	Starting compound	Method and conditions	Trace impurities in the product	Reference
1	2	3	4	5
Al	Di-isobutylaluminium hydride	Pyrolysis at 340°	Carbon $< 2 \times 10^{-2}$	21
	Tri-isobutylaluminium	Pyrolysis at 200°	Purity 99.999	50
	Complex of triethyl-aluminium with sodium fluoride	Electrolysis with lead anode	High purity	50
In	Trimethylindium complexes	Electrolysis	Cu 5×10^{-5}, Cd 2×10^{-4}, Tl 1.4×10^{-5} wt.% Fe, Pb, Sn, Ag, Mg, Si, Ni not detected	51,52
Ga	Triethylgallium	Electrolysis	Pb $\ll 1 \times 10^{-4}$, Zn 4×10^{-6}, Cu 8×10^{-6}, wt.% Sn, Mn not detected	51,52
Tl	Organic complexes of thallium salts	Electrolysis	Al 9×10^{-5}, In 8×10^{-4}, Mg 3×10^{-5} wt.% Ag, Cu, Fe, Si not detected	51,52
Ge	Germanium tetra-alkyls	Pyrolysis at 400°	Carbon < 0.1%	53,54
Fe–Ni	Mixed iron and nickel carbonyls	Pyrolysis below 200°	Carbon < 0.001%	55
Fe	Carbonyl iron	Pyrolysis and heating in hydrogen	Ni $1-2 \times 10^{-4}$ C $< 3 \times 10^{-3}$ C 1×10^{-2} S, P, Cu, Mn	7
	ditto	Pyrolysis at 200–300°	Ni, Co, Cr, Mo, Zn, Si not detected	39
Ru	Dicyclopentadienyl-ruthenium	Pyrolysis at 595° in hydrogen	Ru 99.99% pure Fe 1×10^{-2}, Pd $< 5 \times 10^{-3}$, Bi, Si even smaller traces	56
W	Tungsten carbonyl	Pyrolysis at 1000°	Carbon 0.02 wt.%	57
Cr	bis-Cumenechromium	Pyrolysis at 300–400°	Carbon < 0.2%	58
	bis-Ethylbenzene-chromium	Pyrolysis	Al 6×10^{-3}, Fe 3×10^{-3}	59
	bis-Benzenechromium	Pyrolysis	Cu $6,1 \times 10^{-4}$, Mo 1.85×10^{-4}, Sn 6.9×10^{-4}, C 1.06×10^{-1}, O 2.04×10^{-2}, H 5.7×10^{-4} N 2.16×10^{-3}; Al, Cd, Fe, Mg, Si not detected	18
Mo	Molybdenum carbonyl	Pyrolysis and heating in hydrogen	Carbon 1×10^{-2}%	38
Mo	ditto	Pyrolysis in an electric field at 600–1200°	Carbon $< 1 \times 10^{-3}$%	36
Ni	Nickel carbonyl	Pyrolysis in the presence of hydrogen sulphide below 100°	C 0.01%	60,61
Ni	Nickel carbonyl	Pyrolysis and heating in wet hydrogen	Mg, Si, P, S 1×10^{-3} Co, Zn, 5×10^{-4}, Cd, Sn, Sb, Pb, Bi, Al 3×10^{-4}, Fe 2×10^{-2} C trace	62

Table 5 (cont'd)

Element or compound	Starting compound	Method and conditions	Trace impurities in the product	Reference
1	2	3	4	5
Ga	Tri-isobutylgallium	Pyrolysis at 200°	Zn $< 1 \times 10^{-3}$, Ag 2×10^{-4}, Cu 4×10^{-5}, Al 1×10^{-4}, Ni $< 1 \times 10^{-3}$, Fe $< 1 \times 10^{-3}$, Cr $< 1 \times 10^{-3}$, Mg 4×10^{-5}, Mn $< 1 \times 10^{-4}$	5
SiO_2	Tetraethoxysilane	Hydrolysis and heating at 650–750°	Al $3-8 \times 10^{-6}$, Fe 2×10^{-6} Mg $2-8 \times 10^{-6}$ Mn $1 \times 10^{-6}-3 \times 10^{-6}$ Cu $2 \times 10^{-6}-8 \times 10^{-7}$, Pb $\sim 5 \times 10^{-6}$, B 2×10^{-6}	17
HfO_2	Hafnium tetra-amyloxide	Hydrolysis, 24 h drying at 50°, 0.5 h heating at 250°	99.995%	63
Al_2O_3	Aluminium tri-iso-propoxide	Hydrolysis	Cu 7×10^{-5}, Mg 4×10^{-4}	5,6
Ta_2O_5	Tantalum penta-ethoxide	Hydrolysis	Ag $< 4 \times 10^{-4}$, Ti $< 3 \times 10^{-4}$, Fe 5×10^{-4}, Pb $< 1 \times 10^{-4}$, Mn $< 2 \times 10^{-5}$	5,6
Nb_2O_5	Niobium penta-ethoxide	Hydrolysis	Ag $< 1 \times 10^{-5}$, Fe 3×10^{-4}, Pb $< 2 \times 10^{-3}$, Mn $< 2 \times 10^{-4}$	5,6
$BaTiO_3$	Barium isopropoxide, titanium tetra-t-amyl-oxide	Hydrolysis	99.98%	44
$HfTiO_4$	Hafnium tetra-amyloxide, titanium tetra-amyloxide	Hydrolysis, 12 h drying at 50°, heating at 580°	99.95% Co $< 1 \times 10^{-3}$, Na $< 5 \times 10^{-3}$, Si $< 3 \times 10^{-3}$, Fe $< 3 \times 10^{-3}$	64
$HfO_2Y_2O_3$	Hafnium tetra-amyloxide, yttrium tri-isopropoxide	Hydrolysis, 12 h drying 60°, 0.5 h heating at 550°	99.95%	65
GaAs	Trimethylgallium, arsine	Pyrolysis	Si 8.6×10^{-5}, S 3.4×10^{-5}, Fe 6.2×10^{-5}, Cu 1×10^{-5}, Zn 4×10^{-5}, C 2×10^{-3}, Ni 1.7×10^{-5}, O 2.4×10^{-3}	10
CdS	Dimethylcadmium, hydrogen sulphide	Pyrolysis	Semiconductor purity	47–49
	ditto	Reaction in solution		46
AlAs single crystal	Trimethylaluminium	Thermal decomp. at 700° in arsine	Semiconductor purity	67
AlP single crystal	ditto	Thermal decomp. at 700° in phosphine	ditto	67
GaP single crystal	Triethylgallium, triethyl-phosphine	Thermal decomp. at 420° of a mixture of tri-ethylgallium and triethyl-phosphine	"	68
ditto	Trimethylgallium	Thermal decomp. at 700° of tri-methylgallium in the presence of phosphine	"	9
AlN	Trimethylaluminium	Decomp. at 1200° of trimethyl-aluminium in ammonia	"	69
GaN	Trimethylgallium	Decomp. at 925–975° in ammonia	"	69
Fe_2O_3	Iron carbonyl	Oxidation	High purity	7
Ge	Tetraethylgermanium	Thermal decomp. at 820° in argon–hydrogen mixture	Semiconductor purity no carbon detected	66

A study of the thermal decomposition of tri-isobutylaluminium

$$[(CH_3)_2CH{-}CH_2]_3Al \rightarrow 3(CH_3)_2C{=}CH_2 + {}^3/_2H_2 + Al$$

has shown[40] that a method of purification of aluminium similar to the carbonyl iron process could be developed by combining the dissolution of technical-grade aluminium in isobutylene in the presence of hydrogen with the decomposition of isobutylaluminium. Some complications arise from the possible contamination of the aluminium with carbon, but the carbon content can be made as low as 2×10^{-2}% by suitable choice of the conditions under which the tri-isobutylaluminium is decomposed[21].

Pure metal oxides and other compounds can be prepared from MOC by methods such as thermal decomposition in the vapour phase of one (or several) compounds, reaction of MOC in solutions or in the vapour phase with oxygen or with compounds having labile hydrogen atoms (hydrogen sulphide, arsine, stibine, phosphine), hydrolysis in the vapour phase or in solution, or decomposition in the plasma of a gas discharge.

Depending on the conditions under which the MOC is decomposed, oxides and semiconducting compounds can be obtained in the form of powders, films, or epitaxially grown layers.

The most convenient sources of pure oxides are metal alkoxides and salts of organic acids.

The hydrolytic decomposition of alkoxides is widely used for the preparation of high-purity metal oxides. This method yields not only powdered oxides and mixed oxides, but also thin films for coating optical surfaces, for protective coatings, and for use as diffusion sources in semiconductor technology[41].

The hydrolytic method has been used to prepare very pure oxides of silicon[17], germanium[42], magnesium, aluminium, and titanium[43]. Very pure mixed oxides and compounds can be obtained by hydrolysing several alkoxides simultaneously. Thus, the hydrolysis of a mixture of barium isopropoxide and titanium tetra-amyloxide yields[44] barium titanate of 99.98% purity and 50–100 Å particle size:

$$Ba(OC_3H_7)_2 + Ti(OC_5H_{11})_4 + 3H_2O \rightarrow BaTiO_3 + 2C_3H_7OH + 4C_5H_{11}OH.$$

The uniformity and stoichiometric composition of the product were confirmed by chemical analysis and electron microscopy. The powder, dried at 50° in an inert gas atmosphere, was shown to have the barium titanate structure by X-ray diffraction analysis and i.r. spectroscopy.

Powders or films consisting of mixed oxides in the required proportions can be prepared from the alkoxides of Group IV elements such as silicon and titanium, and also aluminium. Simultaneous hydrolysis of solutions of tetraethoxysilane and compounds of other elements has been used to prepare powders and glasses of various compositions[45]. Calculated compositions of the oxides in solution were found to agree satisfactorily with the experimentally observed compositions of the powders obtained by hydrolysis[45].

The film-forming component (e.g. the alkoxide) must be suitably chosen to ensure that the oxide is deposited as a film. Tetraethoxysilane and some inorganic compounds are used in solution in polar organic liquids, aqueous alcohol, or acetone–water mixtures. The water content varies between 0.1 and 10–20%, depending on the nature of the film-forming compound[41]. Mixtures of polar and non-polar solvents can also be used to prepare films from mixtures of several compounds.

One of the distinguishing features of the use of MOC for the preparation of semiconducting compounds (in contrast to the use of inorganic compounds) is that the purity problems are less intractable. This is because the preparation of semiconductor materials from MOC usually involves lower temperatures than the preparation of the same materials from inorganic compounds, thus minimising the danger of contamination from the material of the apparatus. Furthermore, the selectivity of the methods of preparation of the MOC (discussed in Section II) ensures that many undesirable impurities are eliminated from the starting material.

Like the oxides, other compound semiconductors can be prepared from MOC by decomposition in solution or in the vapour phase. The conditions under which the decomposition is carried out are determined mainly by the form in which the semiconductor is required (powder, deposited film, or epitaxially grown layer).

Pure metal chalcogenides can be prepared by treating MOC in solution with hydrogen sulphide. Hanschild and Glemser[46] have obtained very pure cadmium sulphide by the reaction between dimethylcadmium and hydrogen sulphide in liquid propane:

$$(CH_3)_2Cd + 2H_2S \rightarrow Cd(SH)_2 + 2CH_4$$
$$Cd(SH)_2 \rightarrow CdS + H_2$$

The cadmium hydrogen sulphide decomposes at −(40–50)°; the last traces of hydrogen sulphide are removed by heating the product in a vacuum. The method yields material free from traces of other metals, and it can be used to prepare other binary compounds.

The preparation of pure semiconductor materials from MOC is particularly attractive when the product is required in a special form (for example, an epitaxially grown layer). Epitaxial layers of $A^{III}B^{VI}$ and $A^{III}B^{V}$ semiconductor compounds and of their solid solutions can be prepared by decomposing a MOC in the vapour phase in the presence of the appropriate hydride at a temperature suitable for the growth of a monocrystalline layer.

Thus, epitaxial structures of gallium arsenide have been prepared[9,10] by the thermal decomposition of gallium alkyls in the presence of arsine. The impurity level of the gallium arsenide with respect to Si, S, Fe, Cu, and Zn was 10^{-4}–10^{-5}. It is interesting to note that the carbon contamination in these layers of gallium arsenide[10] is of the same order ($\sim 2 \times 10^{-3}$%) as in the layers prepared from gallium and arsenic chlorides: hence, this contamination cannot be due to the carbon from the MOC. Epitaxial structures of cadmium and zinc sulphides, selenides, and tellurides, of semiconductor purity, have been obtained by the thermal decomposition in the vapour phase of dimethylcadmium and diethylzinc in the presence of hydrogen sulphide or hydrogen selenide, or of dimethyltellurium[47–49].

We may conclude from these examples of the preparation of high-purity materials that the decomposition of MOC is a very promising method of preparation of pure metals, oxides, and compound semiconductors. It lends itself to the production of these materials not only in a pure form, but also in the special configurations required in electronics technology. Rapid developments of the MOC method can be expected in the near future.

Various examples of the preparation of high-purity materials from MOC are listed in Table 5 together with the appropriate conditions.

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In conclusion, we have established that the thermal decomposition of MOC is a powerful method of preparation of various substances in a high state of purity as coatings, films, and single-crystal layers. The method can be applied also to refractory materials. Rapid developments, leading to widespread practical applications, can be expected.

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Paramagnetic Shift Reagents in Nuclear Magnetic Resonance Spectroscopy

I.Ya.Slonim and A.Kh.Bulai

The physical foundations and the applications of a new method in nuclear magnetic resonance spectroscopy—the simplification of spectra by means of paramagnetic shift reagents, complexes of lanthanides with diketones—are examined, and data given on the properties of the most widely used reagents. The discussion covers the mechanism of interaction of the shift reagent with the organic compound (substrate), the dependence of the displacement of the signals on the concentration of the components and the temperature, the equilibrium in the reagent-substrate system, the effect of the nature of functional groups in the substrate, of the lanthanide ion, and of the ligand in the reagent on the magnitude of the shift in the n.m.r. spectra, the dependence of the shift and the line width on geometrical factors, and the effect of the shift reagent on spin-spin coupling constants. The use of shift reagents in the nuclear magnetic resonance of protons and other nuclei is considered briefly. The paper includes a summary of compounds whose spectra have been studied in the presence of shift reagents and also 348 references.

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I. INTRODUCTION

Nuclear magnetic resonance spectroscopy has become probably the most powerful method for determining the structure of organic compounds, including polymers and biopolymers. However, the information content of proton magnetic resonance spectra is substantially diminished by the fact that the protons in methine, methylene, and methyl groups unaccompanied by electronegative atoms give signals having closely similar chemical shifts in the range 0.8–2.5 ppm. A new and extremely effective method, which in several cases completely overcomes difficulties due to the overlapping of signals, is the use of paramagnetic shift reagents.

The effect of paramagnetism on nuclear magnetic resonance was detected soon after discovery of the latter [1]. Detailed theoretical and experimental studies of n.m.r. in paramagnetic systems have been reviewed [2-12]. Successful attempts were made to use nickel(II) and cobalt(II) complexes as shift reagents [13,14], but these compounds have not found wide application. A decisive step for development of the method was the change to lanthanide derivatives—complexes of europium [15,16], praseodymium [17], and other lanthanides [18-24] with 2,2,6,6-tetramethylheptane-3,5-dione, complexes with fluorine-containing [25] and with optically active [26-29] diketones.

Lanthanide shift reagents—complexes of tervalent ions Ln^{3+} with β-diketones—are Lewis acids. In solution they form complexes (adducts) with organic molecules (substrates) containing atoms having a lone pair of electrons (oxygen, nitrogen, sulphur, phosphorus), the substrates being Lewis bases. The paramagnetic ion displaces the lines in the n.m.r. spectrum. Because of rapid exchange between free and complexed molecules the observed spectrum is intermediate between those of the free and the bound substrate.

The Review will survey the physical principles underlying the action of paramagnetic shift reagents, discuss the effects of various factors on the n.m.r. spectrum of the substrate—reagent system, and briefly consider the application of paramagnetic shift reagents in organic and polymer chemistry.

II. PARAMAGNETIC SHIFT REAGENTS USED IN n.m.r. SPECTROSCOPY

Among the many known complexes of lanthanides (several hundreds were tested in a single study [25]!) only a few have found practical use as paramagnetic shift reagents. This is because shift reagents should satisfy several requirements. Such properties as great coordinating power with substrates, magnetic anisotropy, a ligand of great bulk (in order to fix the relative positions of substrate and reagent molecules in the adduct), and short electronic relaxation time (to keep the spectral lines narrow) are of considerable importance. It is also necessary that the substance should be sufficiently stable in the air, soluble in organic solvents, etc. Tables 1–3 list the properties of β-diketonatolanthanide paramagnetic shift reagents. Salts—chlorides and chlorates—can be used in aqueous solutions, and lanthanide nitrates in acetone solutions [30-34].

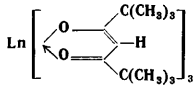
The solubility of the trisdipivalomethanatoeuropium(III) complex in carbon tetrachloride, hexadeuterobenzene, and deuterochloroform at room temperature is respectively [35] 200–300, 100, and 200–300 mg ml^{-1}. The solubility increases in the presence of a polar substrate [36]. The corresponding ytterbium complex is more soluble [37], as is also tris-6,6,7,7,8,8,8-heptafluoro-2,2-dimethyloctane-3,5-dionatoeuropium(III), up to 400 mg ml^{-1} in carbon tetrachloride [25]. This last anhydrous complex, the corresponding praseodymium compound, and the tristetramethylheptanedionatoeuropium complex are strongly hygroscopic [25,38], and should therefore be kept over phosphorus pentoxide in a vacuum desiccator [25]. The solvents used in work with the shift reagents should be especially carefully dried and freed from acidic impurities: chloroform is treated with molecular sieves [35]; carbon tetrachloride is stored over caustic soda and redistilled [42].

III. EFFECT OF PARAMAGNETIC SHIFT REAGENTS ON n.m.r. SPECTRA

1. Shifts of Signals in Spectra

The shift in the n.m.r. signal of the substrate in the presence of lanthanide shift reagents is caused by the local magnetic field produced by the ion at the site of the nucleus. Most authors consider that the main contribution to the shift is made by so called "pseudocontact" (dipole) interaction appearing when the magnetic susceptibility of the complex is anisotropic: the field due to the lanthanide is not then averaged out by the molecular motion.

Table 1. Dipivaloylmethane complexes Ln dpm$_3$—tris-2,2,6,6-tetramethylheptane-3,5-dionatolanthanide complexes



(preparation [37,39,40] and properties [35,38,41,42]).

Ln	Colour	M.p., °C	Magnetic moment, β	Nuclear magnetic resonance spectrum: without substrate, t-butyl δ, ppm	without substrate, line width, Hz	with cyclohexanone, t-butyl δ, ppm	with cyclohexanone, line width, Hz
Pr	light green	222—224	3.7	0.6	40	2.8	2
Nd	violet	215—218	3.7	0.8	16	2.1	10
Sm	white	196—199	2.0	1.08	7	1.2	6
Eu	yellow	187—189	3.4	0.48	10	—0.5	5
Gd	white	182—184	7.6	0.9	1500	1.8	800
Tb	white	177—180	9.6	17.4	250	16.0	170
Dy	white	180—184	10.3	17.7	180	21.9	130
Ho	yellowish white	180—183	10.0	5.30	180	7.3	180
Er	pink	179—181	9.3	—3.6	250	—6.2	70
Tm	white	172—174	7.2	12.8	400	15.2	240
Yb	white	167—169	4.3	—0.3	60	—1.9	20

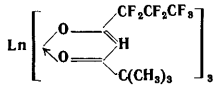
When the rate of molecular reorientation is large in comparison with the n.m.r. line width expressed in the same units, but small compared with the rate of electronic relaxation, and the complex has axial symmetry, the shift is given by the formula [46-49]

$$\delta_i = -10^6 \cdot \frac{1}{3N_A}(\chi_{M\parallel} - \chi_{M\perp})\frac{3\cos^2\theta_i - 1}{r_i^3} \qquad (1)$$

where δ_i (in ppm) is the shift in the signal for the ith nucleus, N_A is Avogadro's number, $\chi M\parallel$ and $\chi M\perp$ are the components of the molar magnetic susceptibility parallel and perpendicular to the symmetry axis, r_i is the length of the vector $\vec{r}_i$ between the paramagnetic ion and the ith nucleus, and θ_i is the angle between this vector and the principal magnetic axis of the complex.

The magnetic susceptibility depends on the electronic configuration of the paramagnetic ion, the ligand field, and the temperature. Equations expressing the pseodocontact shift in terms of the anisotropy of the g-factor were obtained by McConnell and Robertson [50] for ions whose magnetic properties obey the Curie law. More complicated expressions are obtained [49,54-57] for the lanthanide ions, especially for Eu^{3+}, in which the ground state (the $^7F_0$ level) is diamagnetic, and paramagnetism arises only from the excited state $^7F_1$. [51-53] Comparison with experiment shows satisfactory agreement [48,57], although difficulties are caused by the fact that magnetic susceptibilities measured on single crystals [48,58] may differ from those of molecules in solution, and furthermore the magnetic susceptibility may change on coordination of the shift reagent with the substrate [38,59,60]. The mainly pseudocontact (dipole) nature of the shift caused by lanthanide shift reagents is confirmed also by the linear dependence of the shift on the geometric factor $(3\cos^2\theta_i - 1)/r_i^3$ (see below), by the identity of proton and carbon-13 shifts in the presence of tristetramethylheptanedionatoeuropium [61,62], by the fact that the shift and the anisotropy of the g-factor have the same sign [19], and by the constancy of the ratio of shifts in the presence of the above complex to those in the presence of the corresponding praseodymium complex for several compounds [63].

Table 2. Tris-6,6,7,7,8,8,8-heptafluoro-2,2-dimethyloctane-3,5-dionatolanthanide(III) complexes Ln fod$_3$



(preparation [43]).

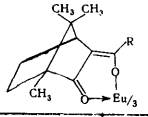
Ln	Colour	Melting point, °C: anhydrous	monohydrate
Eu	white	205—212 (decomp.)	59—67
Pr	green	218—225 (decomp.)	218—225 (decomp.)

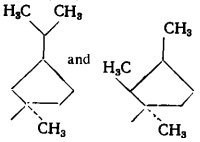
If the electron spin density of a paramagnetic ion is delocalised, and is transmitted through a system of chemical bonds to the nucleus, a contact shift in the n.m.r. signal is observed [64]:

$$\delta_i = -10^6 \cdot A_i \frac{\gamma_e}{\gamma_n} \frac{g\beta S(S+1)}{3kT} \qquad (2)$$

where γ_e and γ_n are the gyromagnetic ratios of electron and nucleus, A_i is the isotropic hyperfine electron–nucleus coupling constant, g is the g-factor, β is Bohr's magneton, S is the spin quantum number of the electron, k is Boltzmann's constant, and T is the absolute temperature.

Table 3. Optically active paramagnetic shift reagents—tris-3-alkylhydroxymethylene-(+)-camphorato-europium(III) complexes



Alkyl R	Preparation—Ref.
$(CH_3)_3$—C—	26
CF_3—	28, 44, 45
$CF_2CF_2CF_3$	29
	27

The contact shift usually plays no great part in changing the n.m.r. spectra in the presence of lanthanide shift reagents. The presence of contact interaction is taken into account only in certain cases—for nuclei situated beside a coordination site, e.g. protons in the *geminal* position to a hydroxy-group [66,67] protons [68,69] and carbon nuclei [70] in strong Lewis bases having a π-bond system in the presence of shift reagents that are strong Lewis acids, and also with nitrogen-14 and phosphorus-31 nuclei.

Pseudocontact and contact interactions displace the signals in the n.m.r. spectra only of those substrate molecules that form an adduct with the paramagnetic shift reagent molecules. In addition, the introduction of a paramagnetic additive produces a large general upfield displacement of the whole n.m.r. spectrum of the solution, owing to a change in the magnetic susceptibility of the solution [71]:

$$\delta_l = 10^6\left[\chi - \chi_0 - \frac{\chi_0 (d_0 - d)}{m}\right]\frac{2\pi m}{3} \qquad (3)$$

where χ and χ_0 are the magnetic susceptibilities (g^{-1}) of the paramagnetic compound and the solvent, d and d_0 are the densities of solution and solvent, and m is the mass of the paramagnetic compound in 1 ml of solution. This shift need be taken into account only when an external standard is employed. The signal of an internal standard (tetramethylsilane) is displaced together with the whole spectrum: hence chemical shifts reckoned from the standard do not change.

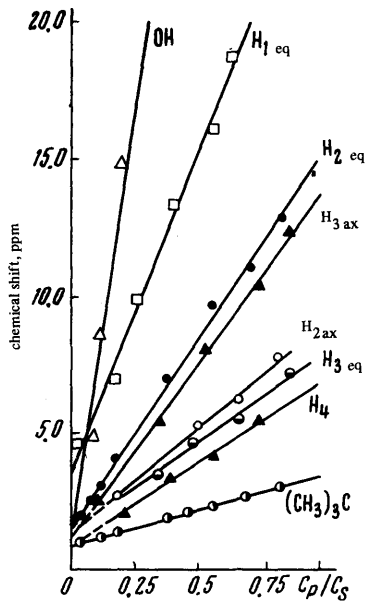
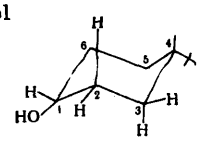


Figure 1. Dependence of chemical shift of protons in *cis*-4-t-butylcyclohexanol



dissolved in $CDCl_3$ in presence of Eudpm$_3$ on the ratio Cp/Cs (frequency 100 MHz and room temperature) [36].

2. Dependence of Shift on Composition of Solution

The shift δ of signals in the presence of a shift reagent is to a first approximation proportional to the ratio of the molar concentration of paramagnetic reagent Cp to substrate concentration Cs (Fig. 1). It has been proposed [36] that the shifts of different protons be compared by using the slopes of the linear plots of δ against Cp/Cs, i.e. by the "specific shifts" or shifts extrapolated to the ratio $Cp/Cs = 1$. For example, this shift ΔEu for the tris-tetramethylheptanedionatoeuropium complex in a solution of *cis*-4-t-butylcyclohexanol in deuterochloroform (Fig. 1) has the values 78.7, 21.7, and 1.8 ppm for OH, $H_{(1)}$, and $(CH_3)_3C$ respectively. Values of the specific shifts ΔEu, ΔPr (for the corresponding praseodymium complex), etc. are given in many papers (see reviews [72-80]). However, they are not true constants: variation in substrate concentration over the range 0.2–0.5 M produces changes in ΔEu of ±15%; values of ΔEu for alcohols and amines are 10% smaller in hexadeuterobenzene, and 20–25% smaller in deuterochloroform, than in carbon-tetrachloride solutions [35].

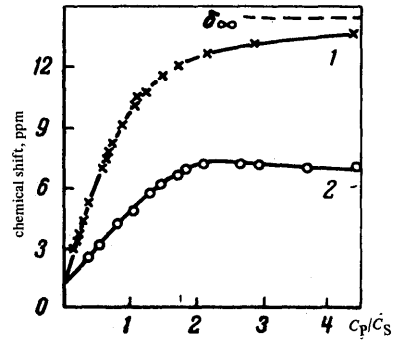


Figure 2. Dependence of chemical shift of signals in n.m.r. spectrum in presence of Eufod$_3$ on Cp/Cs ratio: 1) 0.0183 M t-butyl alcohol, calculated for K = 208 M^{-1}; [84] 2) 0.0130 M t-butylamine.

A departure from the linear dependence of δ is observed at ratios $Cp/Cs \geqslant 0.6$–0.8, the shift reaching a limiting value or even decreasing on further addition of the shift reagents [25,81-84] (Fig. 2). This dependence of the shift on solution composition is due to equilibrium complex formation

$$qP + lS \rightleftarrows P_qS_l \qquad (4)$$

with the constant

$$K = C_{PS}/(C_P - qC_{PS})^q(C_S - lC_{PS})^l \qquad (5)$$

where C_{PS} is the concentration of the complex P_qS_l. When the reagent causes rapid exchange, the shift in the substrate signal is

$$\delta = l(C_{PS}/C_S)\,\delta_\infty \qquad (6)$$

where δ_∞ is the shift of the bound substrate. At low Cp/Cs ratios almost all the reagent in solution is combined with the substrate; when the ratio approaches q/l an appreciable fraction of the reagent remains uncombined, and the dependence of δ on Cp/Cs becomes non-linear.

The parameters characterising the shift reagent–substrate system (composition of complexes (q/l), the constant K, and the shift of the bound substrate δ_∞) can be evaluated from the spectra. Methods for calculating complex-formation equilibria from n.m.r. spectra have been worked out in detail (see for instance reviews [85-88]). But difficulties are encountered in applying these methods to solutions of shift reagents. Variation of the concentration ratio of the components is restricted at high concentrations by the limited solubility of the reagents and at low concentrations by the high sensitivity to impurities, especially to small quantities of water. Calculations are complicated also by possible dimerisation of the complexes in solution [25,38,89-92].

Composition of complexes

In the trisdiketonates the Ln^{3+} ion has the coordination number 6. It can acquire up to three ligand molecules, thereby increasing its coordination number to 9; adducts of Eu dpm$_3$, Pr dpm$_3$, and other lanthanide complexes with pyridine and other substrates containing one, two, and three molecules of the Lewis base have been isolated as crystals [41,93,94]. The composition of a complex in solution can be determined by a method of continuous variation [95]. It follows from Eqn. (6) that

$$C_S\delta = C_{PS}l\delta_\infty \qquad (7)$$

If the concentrations C_P and C_S are varied while their sum is maintained constant, the graph of $C_S\delta$ plotted against $C_P/(C_P + C_S)$ passes through a maximum at

$$C_P/(C_P + C_S) = l/(q + l)$$

This method has established [84] formation of a 1 : 1 complex in the t-butyl alcohol–Eufod$_3$ system, and of 1 : 1 and 1 : 2 complexes in the corresponding t-butylamine system. The displacement of the signal is smaller in the 1 : 2 complex than in the 1 : 1 complex, which leads to the apparent paradox of a decrease in the shift on the addition of excess of the shift reagent (Fig. 2, curve *2*). If exchange in solution is slow, e.g. in the deuterated Eufod$_3$–dimethyl sulphoxide system at −80 °C, two separate signals are obtained—from free and bound substrate—the areas of which give the composition of the complex directly [96] as 1 : 2. A case of stepwise formation on 1 : 2 and 1 : 1 complexes has been examined [97].

The composition of the complex can sometimes be assessed from indirect data. For example, addition of optically active (R)-*N*-methyl-1-phenylethylamine to a solution containing Eu dpm$_3$ and racemic 1-phenylethylamine splits the signal of the CH–NH$_2$ protons of the latter [27]. Obviously this is possible only if an adduct containing both amines, e.g. 1 : 1 : 1, is at once formed with the shift reagent.

Complex-formation constant K and limiting shift δ_∞

These parameters can be found by selecting (by means of an electronic computer) values giving minimum deviation between the measured shifts and the $\delta = f(C_P/C_S)$ curve calculated by simultaneous solution of Eqns. (5) and (6) (Fig. 2, curve *1*). Good agreement confirms the formula for the complex adopted in the calculation.

With small C_P/C_S ratios the equimolecular complex is formed preferentially, and from Eqns. (5) and (6) with $C_P \ll C_S$ we obtain

$$\frac{1}{\delta} = \frac{C_S}{\delta_\infty C_P} + \frac{1}{K\delta_\infty C_P}. \qquad (8)$$

The graph of $1/\delta$ against C_S with C_P constant is a straight line [98,99]; its slope gives the parameter K, and the intercept made on the vertical axis yields δ_∞.

Table 4. Formation constants of complexes of shift reagents with substrates.

No.	Shift reagent	Substrate	Solvent	Temp., °C	K, M^{-1}	Ref.
1	Eu (FOD)$_3$	t-butyl alcohol	CCl_4	room	280±10	84
2	Eu (FOD)$_3$	propan-2-ol	CCl_4	32	97±8	98
3	Eu (FOD)$_3$	oxolan	CCl_4	32	57±3	98
4	Eu (FOD)$_3$	butan-2-one	CCl_4	32	32±3	98
5	Eu (FOD)$_3$	isopropenyl acetate	CCl_4	32	27±3	98
6	Eu (FOD)$_3$	allyl acetate	CCl_4	32	26±3	98
7	Eu (FOD)$_3$	cholesterol	CCl_4	room	237	104
8	Eu (FOD)$_3$	n-propylamine	CCl_4	ditto	>100	105
9	Eu (FOD)$_3$	neopentanol	CCl_4	»	>100	105
10	Eu (FOD)$_3$	acetone	CCl_4	»	12	106
11	Eu (DPM)$_3$	n-propylamine	$CDCl_3$	»	11.5–12.9	99
12	Eu (DPM)$_3$	n-propylamine	$CDCl_3$	»	34.2	105
13	Eu (DPM)$_3$	neopentanol	$CDCl_3$	»	6.2–6.5	99
14	Eu (DPM)$_3$	neopentanol	$CDCl_3$	»	9.7	105
15	Eu (DPM)$_3$	propiophenone	$CDCl_3$	40	15.0	69
16	Eu (DPM)$_3$	ethyl benzoate	$CDCl_3$	40	20.6	69
17	Eu (DPM)$_3$	2-phenylethanol	$CDCl_3$	40	101	69
18	Eu (DPM)$_3$	4-methylpyridine	$CDCl_3$	40	140	69
19	Eu (DPM)$_3$	2,4,6-trimethylpyridine	$CDCl_3$	40	10.8	69
20	Eu (DPM)$_3$	trimethylcholestanol	$CDCl_3$	room	61.5	107
21	Eu (DPM)$_3$	methyladamantanone	$CDCl_3$	ditto	250	89
22	Eu (DPM)$_3$	pyridine	$CDCl_3$	27	97	108
23	Eu (DPM)$_3$	quinoline	$CDCl_3$	20	14	109
24	$EuCl_3$	ribofuranosyladenine monophosphate	D_2O	28	10±2	30
25	$HoCl_3$	ribofuranosyladenine-phosphate	D_2O	28	6±2	30
	$EuCl_3$	ribofuranosylthymine monophosphate	D_2O	28	17±3	30

Published values of K are listed in Table 4. Because of the above difficulties, they evidently cannot be regarded as entirely trustworthy. Relative determinations based on competition between substrates [100] are probably more reliable (subsection 7).

3. Dependence of Shift on Temperature

The displacement of signals caused by a shift reagent diminishes on heating. Such observations have been made for many systems, e.g. pentanol [101], heptan-2-one [42], poly(methyl methacrylate) [102], and terpenoids [81] in the presence of tristetramethylheptanedionatoeuropium, and alcohols and amines in the presence of an optically active shift reagent [29]. Quantitative measurements are few and contradictory. Tomic [103] found a linear temperature dependence of the shift between 40° and 90 °C for the methylcyclopropylmethanol system, with the slope of the $\delta-T$ straight lines different for different protons and increasing strongly with the concentration of the shift reagent (Fig. 3). The shifts in the spectra of furfuryl alcohol, octanol, and several vinylalkanones have been shown [110] to be proportional to $T^{-1/2}$ between −30° and +60 °C. If the molecular geometry is independent of temperature, a pseudocontact shift should theoretically [49] be proportional to T^{-2} for all lanthanide ions other than Sm^{3+} and Eu^{3+}.

The samarium(III) ion should exhibit a dependence on T^{-1} near room temperature, and the europium(III) ion should show a variation stronger than T^{-1} but weaker than T^{-2}. Departures from theory, observed not only with lanthanide shift reagents but also with transition-metal

complexes[111], are explained primarily by the strong influence of temperature on the equilibrium between free and complexed substrate.

4. Dependence of Shift on Nature of Functional Group in Substrate

The nature of the functional group has a decisive effect on the displacement, since it influences also the complex-formation constant and the interatomic distances and angles occurring in Eqn. (1). Different groups can be compared on the basis of the specific shift ΔEu (Table 5).

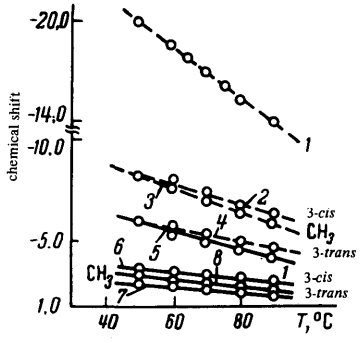
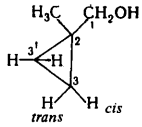


Figure 3. Temperature dependence of chemical shift (on δ-scale) in n.m.r. spectrum of 1-methylcyclopropyl-methanol



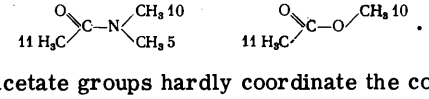
(0.02 M solution in CCl_4) in presence of Pr dpm$_3$: 1–4) 0.09 M; 5–8) 0.05 M.[103]

Table 5. Specific shift ΔEu for various functional groups (0.2–0.5 M solutions in CCl_4 at room temperature)[35].

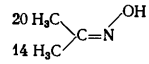
Functional group*	Specific shift, ppm	Functional group*	Specific shift, ppm
$RCH_2\underline{NH_2}$	150	RCH_2CHO	11
$RCH_2\underline{OH}$	100	$RCH_2OCH_2R^1$	10
$RCH_2\underline{NH_2}$	30—40	$RCH_2CO_2CH_3$	7
RCH_2OH	20—25	$RCH_2CO_2CH_3$	6.5
RCH_2COR	10—17	RCH_2CN	3—7
RCH_2CHO	19		

*The proton whose signal is observed is underlined.

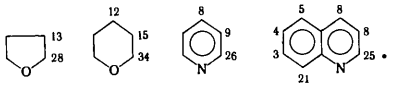
Amide groups bind tristetramethylheptanedionato-europium 4–5 times as strongly as do ester groups[112]; values have been found for substituted amides[113] close to those measured[114] for esters (henceforward numerals accompanying chemical formulae will indicate the values of ΔEu):



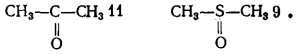
Trifluoroacetate groups hardly coordinate the complex at all[115]. Large shifts are observed with oximes[116,117]:



Similarly with oxygen-containing[114,118] and nitrogen-containing[79] rings:



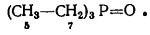
Values of ΔEu for the *N*-oxides of pyridine and quinoline are 30–40% smaller than those for the original heterocycles[119]. Shifts in the spectra of sulphoxides are of the same order as in ketones[114,120]:



Thioacetal groups



do not combine with shift reagents[115]. The latter are successfully used to displace the signals in the spectra of compounds containing phosphoryl groups[83,121,122], e.g. phosphine oxides



Values of ΔEu decrease in the sequence[121]

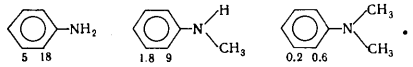
$$P{=}O > C{=}O \text{ (Amides)} > C{=}S \text{ (Thioamides)} > P{=}S.$$

Nitro-groups and phosphines bind shift reagents weakly. Halides and double bonds probably do not interact with lanthanide shift reagents[35].

With compounds having the same functional groups the degree of bonding of the shift reagent depends on basic strength and steric hindrance. This rule is well observed in sulphur-containing compounds[123] and with amines[124] of general formula p-$XC_6H_4NH_2$, where ΔEu increases slowly with pKa of the amine in the sequence of substituents X

$$NO_2 < CN < Br < Cl < H < F < OCH_3.$$

The effect of steric hindrance is seen on comparing aniline, methylaniline, and dimethylaniline, which have closely similar pKa values:



Similar observations have been made with other amines[125] and with ketones and alcohols[126]. Steric hindrance may make the coordination of tristetramethylheptanedionato-europium at a hydroxy-group even less than at an ether group in the same molecule[127]. The degree of binding of the shift reagent is so sensitive to the basicity of the functional group that replacing hydrogen by deuterium *geminal* to a hydroxyl produces appreciable displacement of the signals in the spectrum ("isotope effect")[128–131].

5. Dependence of Shift on Nature of Shift Reagent

The sign and the magnitude of the pseudocontact shift (for a given substrate) are determined by the magnetic anisotropy (value of $\chi M_{\parallel} - \chi M_{\perp}$) of the shift reagent and the stability of the coordinate bond between reagent and substrate. The sign of the above difference depends mainly on the nature of the central lanthanide ion in the complex, and the degree of coordination on the nature of the ligand (diketone). The dependence of the shift on the

nature of the lanthanide has been studied in detail on the series of Ln dpm$_3$ complexes for the proton [18,20,23,24,42,132,133] and carbon-13 [22,61] n.m.r. spectra. The shift varies regularly in the series of lanthanides (Fig. 4) [19]. Complexes of cerium-group lanthanides (praseodymium, europium) give numerically smaller shifts than do those of the yttrium group (terbium, dysprosium, holmium, erbium, thulium, ytterbium), but line broadening is far less (see below).

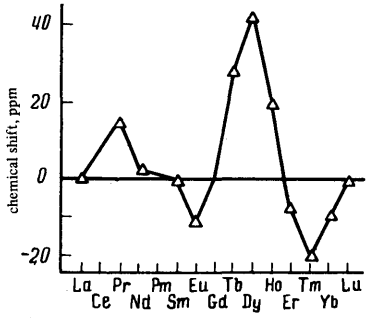


Figure 4. Shift of $H_{(1)}$ proton signal in spectra of n-hexanol (0.8 M solution in $CDCl_3$) produced by lanthanide complexes Ln dpm$_3$ at the ratio Cp/Cs = 0.125. [19]

The effect of the ligand can be observed in the complexes of europium with fluorinated β-diketones [25,134]; increase in the fluorine content is accompanied by an increase in the Lewis acidity (decrease in pK_a) accompanied by increase in the displacements in the n.m.r. spectra. This is especially noticeable in the spectra of substrates that are weak Lewis bases, e.g. ethers [25]. Complexes of lanthanides with pentane-2,4-dione, 1,3-diphenylpropane-1,3-dione, and 1-phenylbutane-1,3-dione are relatively ineffective as paramagnetic shift reagents [35,128,129,135]. This may be due to insufficient bulk of the ligand, low magnetic anisotropy of the complex, or finally a small complex–substrate association constant.

6. Dependence of Shift on Geometric Factors

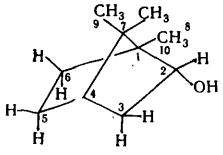
The dependence of the pseudocontact shift on the distance r_i from the given nucleus to the paramagnetic ion and on the angle θ_i between the vector and the axis of the complex, defined by the equation

$$\delta_i = \text{const}\ (3\cos^2\theta_i - 1)/r_i^3$$

is extremely valuable for the employment of shift reagents in practical n.m.r. spectroscopy. Its use enables signals in the spectrum of a molecule of known structure to be assigned comparatively easily; and conversely information on the geometry of the molecule to be obtained if the assignment is known.

In several cases experimental data on the dependence of δ on r and θ for "rigid" cyclic molecules are well described by Eqn. (1). Such results have been obtained, for instance, in the proton magnetic resonance spectra (Table 6) [136] and the carbon-13 n.m.r. spectra [61] for borneol in the presence of tristetramethylheptanedionatopraseodymium, for bicyclic ethers [137] and nitrogen heterocycles [109] in the presence of the europium complex, and for vinylpyridine in the presence of the corresponding complexes of several lanthanides [19].

Table 6. Comparison of specific shifts in spectrum ΔPr with geometric factor for the borneol–Pr dpm$_3$ in CCl_4 solutions at room temperature (100 and 200 MHz) [136].



Proton	*exo*-2H	*exo*-3H	*endo*-3H	4H	*exo*-5H	*endo*-5H	*exo*-6H	*endo*-6H	8CH$_3$	9CH$_3$	10CH$_3$
ΔPr	45.0	16.6	34.2	10.1	10.5	16.0	15.7	35.6	7.78	8.01	17.8
$\frac{3\cos^2\theta_i - 1}{r_i^3 \times \text{const}^{-1}}$	49.0	15.8	30.2	9.84	11.0	16.1	16.0	38.7	7.84	7.88	16.5

The importance of the angle-dependent term in (1) is supported by the fact that signals of nuclei for which $\theta_i \simeq 54°$, e.g. the aromatic protons in t-butylphenylcyclohexanol [138], are not displaced by addition of the europium complex, but when $\theta_i > 54°$ the signals shift in the opposite direction—upfield with the europium complex and downfield with the praseodymium complex [139–144].

Table 7. Position of lanthanide ion in shift reagent–substrate adducts.

Shift reagent	Substrate	Ln to O (N), Å	C-O-Ln (C-N-Ln) angle	Ref.
Eu (DPM)$_3$	4-t-butylcyclohexanol	3—4	180—160	35
Eu (DPM)$_3$	adamantan-2-one	3—4	180—160	35
Eu (DPM)$_3$	quinoline	4.0	180	144
Eu (DPM)$_3$	isoquinoline	3.0	180	144
Eu (DPM)$_3$	pyridine, quinoline	4.0±0.4	180	109
Eu (DPM)$_3$	pyridine	2.9	180	156
Pr (DPM)$_3$	borneol	3.0	126	136
Yb (DPM)$_3$	acrylaldehydes	3.0	180	21
Yb (DPM)$_3$	pyridine	3.0±0.3	180	20

Many attempts have been made to plot the dependence of the shift on separation without considering the angular term, on the assumption that $\delta_i = r_i^{-n} \times$ const. The distance r_i is then measured, not to the lanthanide ion, but to the oxygen or nitrogen atom through which the shift reagent is coordinated [36,40,145–149]. Critical analyses by Rafalski [150] and by Goodisman [151] have shown that values of n = 0.2–3.6 are then obtained, with n = 2 recommended [150] for practical purposes. Such a method of calculation is convenient in not requiring the position of the lanthanide ion in the reagent–substrate adduct to be known, but the procedure should be employed with great caution.

Crystallographic data can be used[152,153] to determine the distance r from nucleus to lanthanide ion, but there is no certainty that distances in solution remain the same as in the crystal. Some complication may arise also from the fact that the principal magnetic axis of the complex does not necessarily coincide with the direction of the bond between lanthanide and donor atom[154]. If we assume that the displacement is given accurately by Eqn. (1), we can determine the position of the lanthanide from the measured shifts. An electronic computer[127] or a graphical method[155] is used to select coordinates of the Ln^{3+} ion at which the deviation from Eqn. (1) is minimal.

Table 8.

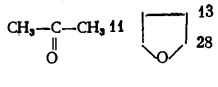
Position of CH_2	1	2	3	4	5	6	7
Shift	1.00	0.58—0.60	0.40—0.42	0.20	0.12—0.14	0.08	0.02—0.05

Table 7 lists data on Ln–O (or Ln–N) distances and C–O–Ln (or C–N–Ln) angles. The appreciable divergence between results obtained by different workers is probably due to errors in measuring the shifts and in determining distances in the models.

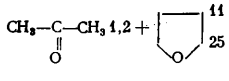
In the case of non-rigid aliphatic molecules interatomic distances are averaged over all possible conformations. Exact calculation of the dependence of δ on r and θ is difficult, and only a gradual diminution in the displacement is observed with distance along the chain from the donor group. Table 8 gives the shifts for successive methylene groups in straight-chain aliphatic alcohols, with the shift due to the hydroxymethyl group taken as unity[35,157]. A methyl group gives a rather smaller displacement than does a methylene group in the same position[101].

7. Displacement due to Shift Reagent in presence of Several Functional Groups

Functional groups of several types may be present in a solution containing a paramagnetic shift reagent. In the simplest case they occur in different molecules: i.e. a mixture of two or more substrates is present. The shift reagent is then distributed between the substrates in proportions depending on the strength of bonding of the reagent and the concentration of the components, with corresponding changes in the shifts of the signals from each substrate. For example[114], the specific shifts



are found for acetone and for oxolan; if, however, the solution contains both compounds, in equimolecular quantities, the values



are obtained: i.e. the displacements have fallen to 11% and 89% of their initial values for acetone and oxolan respectively. From this it may be deduced that oxolan binds tristetramethylheptanedionatoeuropium eight times as strongly as does acetone.

If a solution contains two substrates forming equimolar complexes $PS^{(1)}$ and $PS^{(2)}$ with a shift reagent, we can write for the complex-formation constants K_1 and K_2 and the shifts of the signals $\delta^{(1)}$ and $\delta^{(2)}$ expressions analogous to Eqns. (5) and (6), which contain the concentrations of substrates and complexes together with the displacements of the bound substrates $\delta_\infty^{(1)}$ and $\delta_\infty^{(2)}$. Eliminating concentrations from these equations, we obtain

$$\frac{1}{\delta^{(2)}} = \frac{1}{\delta^{(1)}}\frac{K_1\delta_\infty^{(1)}}{K_2\delta_\infty^{2}} + \frac{K_2 - K_1}{K_2\delta_\infty^{(2)}} \qquad (9)$$

The plot of $1/\delta^{(2)}$ against $1/\delta^{(1)}$ for solutions of varying composition is a straight line of slope $K_1\delta_\infty^{(1)}/K_2\delta_\infty^{(2)}$, making an intercept $(K_2 - K_1)/K_2\delta_\infty^{(2)}$ on the ordinate axis. If values of the parameters K_1 and $\delta_\infty^{(1)}$ for one compound are known, this graph can be used to determine the corresponding parameters for the second compound. This "monitor" method[100] is convenient in not being as sensitive to moisture as direct methods.

When two functional groups are present in the same molecule, but sufficiently far apart not to interact, e.g. at positions 3 and 17 in a steroid molecule[66,149], the same relations hold between coordination at the two groups. The displacement of the signals is then simply the sum of the shifts caused by coordination at each group separately, and can be calculated additively either numerically[149] or graphically[66]. When the complex-formation constants of the two groups differ greatly, the competition between them ensures that the shift reagent combines initially with one group, and only then with the second group on further addition of the reagent. At low concentrations of the reagent, therefore, protons situated near the first functional group are more strongly displaced, but at high concentrations protons beside the second group take over. The signals "overtake" one another on the spectrum; the straight lines corresponding to different protons intersect on the graph of δ as a function of C_P/C_S.[122,158]

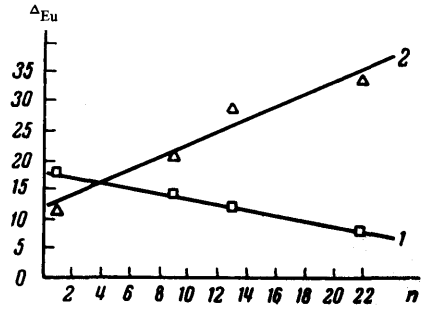
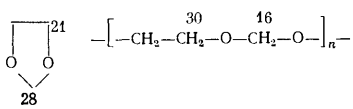


Figure 5. Dependence of specific shift ΔEu on degree of polymerisation n of polyethylene glycols in CCl_4 solution at room temperature (60 MHz) for: 1) terminal CH_2 groups; 2) central CH_2 groups[159].

More complicated relations are observed if the molecule contains different numbers of groups of each type, e.g. for functional groups in the middle and at the ends of a polymer molecule. Thus chain lengthening in the

series of polyethylene glycols $HO[CH_2CH_2O]_nH$ is accompanied [159] by increase in the proportion of tristetramethylheptanedionatoeuropium coordinated at the ether bonds in the central units, and a diminution of coordination at the terminal hydroxy-groups, with a corresponding variation in ΔEu (Fig. 5). Changes in the distribution of the shift reagent between different functional groups are observed also when the solution is heated: a group which is less effective at room temperature may be more effective at a higher temperature [160].

If two functional groups in a substrate molecule are close together, the displacements are no longer additive [146]. The bonding to the shift reagent and the magnitude of the shift depend on the distance between the groups: e.g. the bonding is considerably stronger for *o*-dimethoxybenzene than for the *meta*-derivative [130]. The displacement is influenced also by stereochemical effects. In polydioxolan, for example, the ethoxyl protons are more strongly displaced in the presence of the above shift reagent, but the formyl protons are more strongly displaced in the monomer [161]:



With a favourable conformation the substrate can evidently interact as a bidentate ligand with the lanthanide ion to form chelate complexes [162,163].

8. Effect of Shift Reagents on Width of Lines in Spectrum

A substantial advantage of lanthanide paramagnetic shift reagents is that, in contrast to complexes of transition metals containing the same ligands [164], they cause little line broadening; even when the signal is displaced by several parts per million, the multiplet structure still remains resolved.

Table 9.

Ln	Pr	Nd	Sm	Eu	Tb	Dy	Ho	Er	Tm	Yb
$\Delta\nu_{1/2}$, Hz	5.6	4.0	4.4	5.0	96	200	50	50	65	12

The broadening of an n.m.r. line in the presence of paramagnetic ions is due to acceleration of the relaxation of the nuclear spin, and also to exchange between bound and free substrate molecules. The main factor determining the substrate n.m.r. line width is the electronic relaxation time T_{1e} of the lanthanide ion. Little broadening may be expected with complexes of ions having short T_{1e} times (Eu^{3+}, Pr^{3+}, Nd^{3+}); ions having large T_{1e} values, e.g. Gd^{3+}, should produce great broadening. Table 9 gives the line widths $\Delta\nu_{1/2}$ of the methyl group in 2-methylpyridine in the presence of tristetramethylheptanedionatolanthanide complexes at the same ratio $C_P/C_S = 0.125$. [19] The broadening in the presence of the gadolinium complex is so great that the spectrum could not be obtained.

The broadening of a line is usually greater the larger the displacement. Broadening is therefore sometimes measured by the ratio $\Delta\nu_{1/2}/\delta$. For example, the values found in the spectra of t-butyl alcohol in the presence of the above lanthanide complexes are listed in Table 10. [18,24]

Table 10.

Ln	Pr	Sm	Eu	Tb	Ho	Yb
$\Delta\nu_{1/2}/\delta$	0.013—0.005	0.02	0.003	0.1	0.02	0.02

The relaxation times T_1M and T_2M of nuclei of a substrate bound in a complex having an anisotropic g-factor and a short T_{1e} time [165] are theoretically [109,166,167] given by the equation

$$\frac{1}{T_{1M}} = \frac{1}{T_{2M}} = \frac{2}{3}\gamma_n^2\beta^2 S(S+1)\frac{1}{r^6} f(g_\parallel, g_\perp, \theta) T_{1e} + \frac{4}{9}\gamma_n\beta S(S+1)\frac{A}{2\pi}(g_\parallel - g_\perp)\frac{3\cos^2\theta - 1}{r^3} T_{1e} + \frac{2}{3}S(S+1)\left(\frac{A}{2\pi}\right)^2 T_{1e} \quad (10)$$

where

$$f(g_\parallel, g_\perp, \theta) = \frac{1}{3}(g_\parallel^2 - 2g_\perp^2) + g_\parallel^2\cos^2\theta + g_\perp^2\sin^2\theta,$$

$g_\parallel$ and $g_\perp$ are components of the g-tensor, and the remaining symbols have the same significance as in Eqns. (1) and (2). The first term in (10) represents dipole–dipole interaction, the second cross relaxation, and the third hyperfine interaction. The dipole contribution predominates, since the hyperfine coupling constant is small (hence according to Eqn. (2) the contribution of contact interaction to the shift is small) in most solutions of the above europium complex and organic compounds. The observed line width is determined by the transverse relaxation time: $\Delta\nu_{1/2} = 1/\pi T_2$. For rapid exchange between bound and free substrate we have theoretically [168-170]

$$\frac{1}{T_1} = \frac{1}{T_1^0} + \frac{\sigma}{T_{1M}} \quad (11)$$

$$\frac{1}{T_2} = \frac{1-\sigma}{T_2^0} + \frac{\sigma}{T_{2M}} + \sigma(\sigma-1)^2\tau_M(2\pi\delta_\infty)^2 \quad (12)$$

where T_1^0 and T_2^0 are the relaxation times in the absence of the chemical shift reagent, σ is the fraction of the substrate combined with the reagent, and τ_M is the mean lifetime of a substrate molecule in the bound state. Equations (11) and (12) can be used to determine τ_M from the measured spin–lattice relaxation time, line width, and shift. The last term in Eqn. (12) is found to make the largest contribution to broadening the signals from protons $H_{(2)}$ and $H_{(8)}$ in quinoline dissolved in carbon tetrachloride in the presence of the europium complex; for this system $\tau_M = 2\times10^{-7}$ s. The strong dependence of line broadening and rate of spin–lattice relaxation on geometric factors (to a first approximation these quantities are proportional to r^{-6}) can be used for the determination of structure [13,30,109].

9. Effect of Shift Reagents on Spin–Spin Coupling Constants

Lanthanide shift reagents have little effect on spin–spin coupling constants J between substrate nuclei. This enables J to be determined by direct measurement of the splittings obtained in first-order spectra after addition of a sufficient quantity of shift reagent to the solution. The invariability of the spin–spin coupling constants has been confirmed by measurements of J_{H-H} in lactones [171],

carbohydrates[172], bicyclic esters[158], nitrogen heterocycles[173], by measurements of J_{Sn-H} in organotin compounds[174], etc.; little change in J has been observed with cyclic alcohols[175].

In several cases the addition of a shift reagent produces a change in J that is not connected with paramagnetism but is due to the effect of complex formation on the distribution of electron density in the molecule[176] or on the conformational equilibrium (see below).

Partial elimination of J_{23} and J_{24} spin–spin coupling in quinoline is observed at high concentrations of the europium reagent[35,109]. This phenomenon is observed also with transition-metal complexes[177–180]. It is analogous to the uncoupling of spins in double resonance, and is explained by a decrease in the relaxation time of the nuclei[181].

10. Effect of Shift Reagents on n.m.r. Spectra of Other Nuclei

The action of paramagnetic shift reagents on carbon-13 and fluorine-19 spectra conforms to the same rules as that on the proton magnetic resonance spectra[65]. Only two special features are evident. Firstly, the displacement of the signals defined by Eqn. (1) is the same as in the latter spectra, but the chemical shifts of other nuclei are far larger than those of protons. Therefore the change in the form of the spectrum is not so striking. Secondly, the n.m.r. spectra of other nuclei are strongly influenced by the change in electronic structure accompanying formation of an adduct with the shift reagent. Therefore the carbon-13 and nitrogen-14 n.m.r. spectra in the presence of the diamagnetic tristetramethylheptanedionatolanthanum exhibit a displacement of the signals comparable with that produced by the paramagnetic europium complex[22,140].

Shift reagents are used in carbon-13 n.m.r. mainly for the assignment of lines by means of the dependence of the displacement on the carbon–lanthanide distance. This method has been applied to the spectra of alcohols[182] and the complicated carbon-13 n.m.r. spectra of natural compounds—cholesterol[183], the alkaloid piperine[140], borneol[61], and isoborneol[62]. Stereoisomers have been identified[184] from the carbon-13 n.m.r. spectra of cyclopentane derivatives in the presence of the europium shift reagent. Shifts in the n.m.r. spectra in the presence of europium, holmium, and neodymium salts in aqueous solution have been used to determine the conformation of mononucleotides[30]. The increased distance between signals in the proton magnetic resonance spectrum substantially facilitates the assignment of signals in the carbon-13 spectrum by selective uncoupling of the $^{13}C-\{^1H\}$ spin–spin interaction[31].

Shift reagents find limited application in fluorine-19 n.m.r., since the introduction of fluorine into an organic molecule diminishes the basicity and weakens coordination of a lanthanide. Perfluorinated alcohols and amines do not coordinate paramagnetic shift reagents. Aromatic amines exhibit[65] the same ratios between shifts in *ortho*- and in *para*-positions as in the proton magnetic resonance spectra.

The nuclei of nitrogen-14 and phosphorus-31 atoms having a lone pair of electrons can interact with paramagnetic shift reagents by a contact mechanism[65]. Use of the tristetramethylheptanedionato-complexes of dysprosium and ytterbium has been recommended for nitrogen-14 n.m.r. (as also for fluorine-19[65]), but the great broadening of the lines makes it very difficult to record the spectra[22,185]. In phosphorus-31 n.m.r. the europium complex has been used to displace the signals in deuterochloroform solution[186], and europium and praseodymium trinitrates in aqueous solution[34].

IV. APPLICATIONS OF PARAMAGNETIC SHIFT REAGENTS IN n.m.r. SPECTROSCOPY

1. Simplification of Spectra

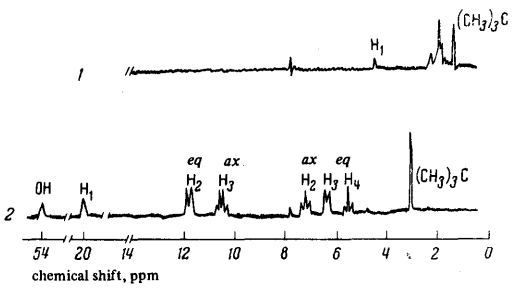


Figure 6. Nuclear magnetic resonance spectrum 100 MHz of *cis*-4-t-butylcyclohexanol in $CDCl_3$ solution: 1) in absence of shift reagent; 2) in presence of Eu dpm$_3$ with $C_P/C_S = 0.7$.[36]

The most important result of the use of shift reagents in n.m.r. spectroscopy is a remarkable simplification of the spectra. The displacement of the signals due to the reagents produces a sharp increase in the chemical shift relative to the spin–spin coupling constant J, which enables first-order spectra to be obtained even for complicated spin systems (Fig. 6)[36].

2. Assignment of Signals

The use of shift reagents makes the assignment of signals in the spectra considerably easier. Their addition separates previously overlapping peaks, so that the signals of protons can be assigned by means of double resonance and analysis of the spin–spin coupling constants.

Above all, however, the method based on the dependence of the displacement on geometric factors is widely used. For example, the structure of *dextro*-camphor shows (Fig. 7) that the distance of the methyl groups from the ketonic oxygen increases in the sequence $10\text{-}CH_3 < 8\text{-}CH_3 < 9\text{-}CH_3$. The distances of the methyl groups from a europium ion coordinated at the keto-group will increase in the same sequence. Therefore the methyl signals that undergo the largest downfield displacement on addition of the shift reagent are assigned to 10-methyl protons, and the least displaced to 9-methyl protons[187]. A similar method has been used to assign signals in the n.m.r. spectra of 1,3-dimethylcyclohexylamine[148], cyclohexyl isocyanide[188], and many other compounds.

3. Determination of Chemical Shifts and Spin–Spin Coupling Constants

Extrapolation to zero shift-reagent concentration of the linear plots of δ against C_P/C_S enables us to determine chemical shifts for those substrate protons whose signals

overlap in the absence of a shift reagent[36,115,172]. Constants J, previously inaccessible because of the superposition of signals—in the n.m.r. spectra of pyrazine derivatives, for example, the couplong constants between protons of the methyl group and *ortho*-, *para*-, and *meta*-protons of the ring[173], and J_{PCH} and J_{PCCH} in those of phosphine oxides[88]—can be obtained from n.m.r. spectra in the presence of shift reagents.

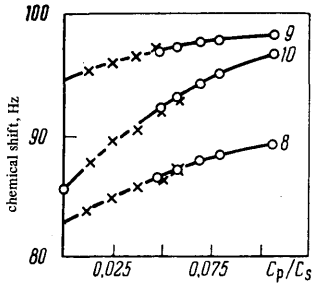
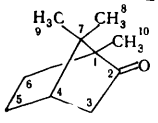
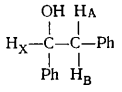


Figure 7. Dependence of chemical shift (at 100 MHz) of 8-, 9-, and 10-methyl groups of (+)-camphor in presence of $Eu\,dpm_3.2C_5H_5N$ on C_P/C_S ratio (solution



in CCl_4 at room temperature)[187].

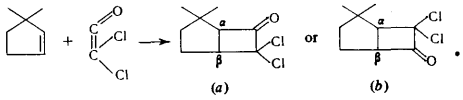
The possibility of evaluating J_{gem} for diastereotopic protons is especially interesting. In the presence of a shift reagent the signals of such protons in the α- and even in the β-position relative to an asymmetric carbon atom are sharply separated[35,115]. Thus the alkyl protons in 1,2-diphenylethanol[35]



give an n.m.r. spectrum of type A_2X, but on addition of the europium shift reagent a spectrum of type ABX is obtained, which enables J_{AB} to be determined.

4. Study of Molecular and Stereochemical Structure

In several cases molecular structure can be determined unambiguously from the dependence of the displacement on geometric factors. For example, dichloroketen can add in two ways to 3,3-dimethylcyclopentene, to yield two structures (*a*) and (*b*)[189]:



The α-hydrogen signal gives a doublet in the n.m.r. spectrum of the reaction products owing to interaction with the β-hydrogen atom, and the β-hydrogen gives a multiplet owing to interaction with the α-hydrogen and with the protons of the five-membered ring. On the addition of tristetramethylheptanedionatoeuropium, which coordinates at the ketonic oxygen, the downfield displacement of the α-hydrogen doublet exceeds that of the β-hydrogen multiplet by 50–100%, which indicates a structure of type (*a*).

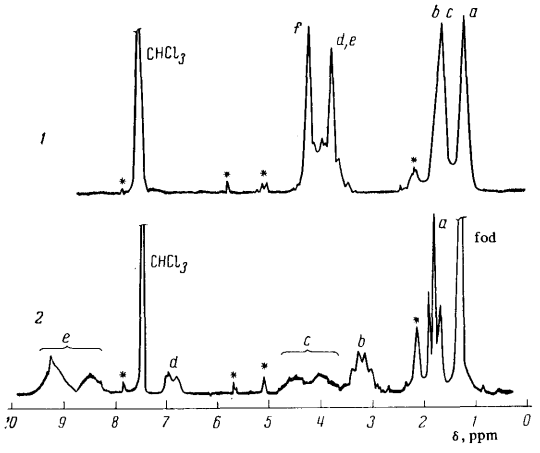
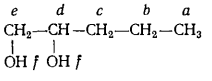


Figure 8. Nuclear magnetic resonance spectrum (at 60 MHz) of pentane-1,2-diol



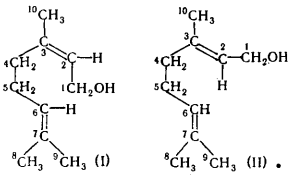
(9 wt.% solution in chloroform at room temperature): 1) in absence of shift reagent; 2) with $Eu\,fod_3$ (C_P/C_S = 1 : 3). The assignment of the lines is shown on the spectrum; the asterisks denote peaks due to impurities and satellites of carbon-13.[190]

Some difficulty has arisen[190] in establishing the structure of the pentanediol isolated from technical furfuryl alcohol. The n.m.r. spectrum (Fig. 8) may correspond to two structures (1,2- and 1,3-diols). When the spectrum is determined in the presence of trisheptafluorodimethyloctanedionatoeuropium the signal of the CH_2–OH group is strongly displaced downfield and is split into two peaks (corresponding to two diastereotopic protons), whereas the signal from the CH_2CH_3 group is not split. This means that the hydroxymethyl group is in the α-position to the hydroxymethylene group: i.e. the 1,2-diol structure is unequivocally proved.

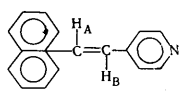
Shift reagents have been used to determine the chemical structure of polycyclic ketones[191], a bicyclic anhydride[192], etc.

Shift reagents are widely used also for identifying geometric isomers. The n.m.r. spectra of nerol (I) and geraniol (II) in the presence of tristetramethylheptanedionatoeuropium show[193] diminishing displacement of the signals of the nerol protons in the sequence $C_{(4)} > C_{(5)} > C_{(10)}$, whereas the corresponding sequence for geraniol is $C_{(10)} > C_{(4)} > C_{(5)}$, which proves that

nerol has the *cis*-configuration (I), and geraniol the *trans*-configuration (II):



In the n.m.r. spectrum of naphthylvinylpyridine



in the presence of the same shift reagent the signals of the vinyl protons no longer overlap those of the naphthalene ring protons, and give a quadruplet of type AB, so that the *cis*- or *trans*-configuration of the compound can be determined from the value of J_{AB} [194].

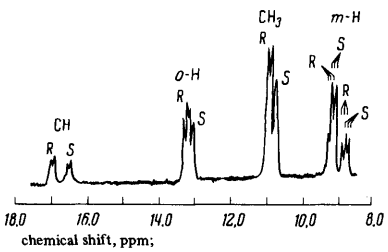
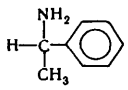


Figure 9. Nuclear magnetic resonance spectrum of solution of mixture of (*R*)- and (*S*)-isomers of 1-phenylethylamine

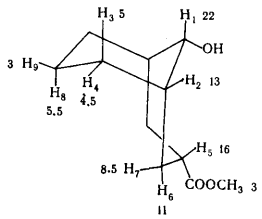


in CCl_4 in presence of 0.15 M tris-3-t-butylhydroxymethylene-(+)-camphoratoeuropium [26].

The enantiomeric purity of compounds—e.g.alcohols [28], sulphoxides [29], amines [26]—can be determined by the use of optically active shift reagents (Table 3). Fig. 9 shows the spectrum of racemic 1-phenylethylamine (mixture of (*R*)- and (*S*)-isomers) in the presence of tris-3-t-butylhydroxymethylene-(+)-camphoratoeuropium [26]. A remarkable feature of this spectrum is the considerable difference between the chemical shifts of corresponding protons in (*R*)- and (*S*)-isomers (from 0.07 ppm for the *para*-protons of the aromatic ring to 0.5 ppm for $CHNH_2$). The signals of the (*R*)-isomer are more strongly displaced than those of the (*S*)-isomer owing to the difference between the stability constants of the complexes they form with the shift reagent. The enantiomeric composition of the mixture is determined from the ratio of the areas of the signals. Tristetramethylheptanedionatoeuropium has been used to identify the *meso*-form and racemic bisphenylsulphinylmethane [195].

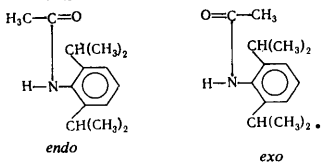
5. Study of Conformation

Paramagnetic shift reagents are used for the conformational analysis of flexible and rigid molecules and for the identification of rotational isomers. Analysis of the shifts of the proton signals in the n.m.r. spectrum of the *cis*-9-hydroxybicyclo[3,3,1]nonane-*endo*-3-carboxylate [158]



in the presence of tristetramethylheptanedionatoeuropium with $C_P/C_S = 0.3$ (when the shift reagent coordinates mainly through the hydroxy-group) shows that the signal of the $H_{(5)}$ proton is considerably displaced downfield, which indicates the boat–chain type of conformation. The conformation of cyclic ketones [196], griseofulvins [197], mononucleotides [30], and bicyclic alcohols [198] has been studied by the use of shift reagents.

It must be borne in mind that formation of a reagent–substrate complex is sometimes able to influence the conformational equilibrium,, e.g. that between *exo*- and *endo*-forms of the substituted amide [142]



In the absence of a shift reagent the ratio of the isomers is *endo*/*exo* = 2/1; addition of 0.1 M of the europium shift reagent changes the ratio of the rotational isomers to *endo*/*exo* = $\frac{1}{2}$. Shift reagents affect also the conformation equilibrium of other amides [133,146], the chair ⇌ chair equilibrium [199], and the equilibrium between carbohydrate anomers [31].

6. Analysis of Mixtures

Impurities can be detected by means of shift reagents, and mixtures of substances having overlapping resonance signals can be analysed by integrating individual peaks in the "stretched" spectrum. This method has been used [101] for the quantitative determination of the components in a binary mixture of 2-methylbutan-1-ol and 2-methylbutan-2-ol, in a ternary mixture of n-pentan-1-, 2-, and -3-ols, and even in a senary mixture of the C_1–C_6 straight-chain alcohols.

7. Study of Polymers

Shift reagents are used to study the stereochemical structure and sequence of units in polymers. The signals from protons in α-methyl and methylene groups are split in the n.m.r. spectrum of poly(methyl methacrylate). The presence of a shift reagent [200] not only facilitates isolation of the signals from α-methyl protons in isotactic (*i*), syndiotactic (*s*), and heterotactic (*h*) triads and the signals from methylene protons in *erythro-mmm* and *threo-rrr* tetrads but also resolves the signal from methoxy-protons into three peaks, corresponding to *i*-, *s*-, and *h*-triads in the polymer chain (Fig. 10). In contrast to this study [200] of the isotactic polymer, an investigation [102] of atactic poly(methyl methacrylate) indicates

that the displacement of the signals of methyl protons diminishes in the sequence i-CH_3 > h-CH_3 > s-CH_3-CH_2, whereas the corresponding sequence for the methoxy-protons is i-CH_3O > h-CH_3O > s-CH_3O. Such a sharp divergence of the results is evidently due to the effect of tacticity on polymer conformation, and hence on the shift, which depends on geometric factors. Resolution of the signal from the protons of a methyl group, under the influence of a shift reagent, into three peaks corresponding to i-, s-, and h-triads has been observed also with poly-(methyl vinyl ether) and polyoxypropylene [201,202].

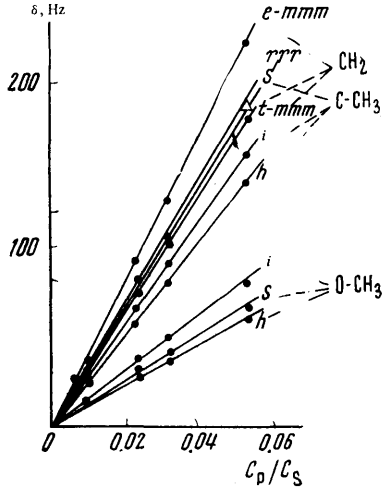


Figure 10. Dependence of shift of signals (at 220 MHz) for protons of poly(methyl methacrylate) in presence of Eufod$_3$ on C_P/C_S (solution in o-dichlorobenzene) [200].

In the n.m.r. spectrum of the trioxan–dioxolan copolymer of general formula $[OCH_2]_x[OCH_2CH_2OCH_2]_y$ the protons of the ethylene oxide group (E) give a singlet, and those of the methylenoxy-group (F) three singlets corresponding to the sequences EFE, EFF, and FFF [161]. On the addition of tristetramethylheptanedionatoeuropium to the solution the three signals due to the methylenoxy-protons coalesce into a single signal, while the peak due to protons of the ethylene oxide group split into three peaks corresponding to the sequences FEFEFEF + FEFEFFF, EFFEFFE + EFFEFFF, and FFFEFFF.

Use of the europium shift reagent enables us to determine the sequence of acid residues in the chain of a copolyester of terephthalic and isophthalic acids with ethylene glycol [203] (the signal from the glycol protons is split into three peaks).

The n.m.r. spectra of glymes—oligomers of formaldehyde and formaldehyde–dioxolan copolymers—in the presence of the europium shift reagent enable a comparative estimate to be made of the basicity of terminal and central oxygen atoms [159], which is important for an explanation of the mechanism of polymerisation. In the spectra of the copolymers $CH_3OCH_2[OCH_2OCH_2CH_2]_nOCH_3$ the signals from methylene protons adjacent to terminal oxygen atoms undergo smaller displacements than with central groups (in Fig. 11 the slope of the straight line a exceeds that of b, and line c is steeper than d): the oxygen atoms obviously become less basic from the middle towards the end of the chain. The signals from protons in methylenoxy-groups in the spectrum of the formaldehyde oligomer $CH_3O[CH_2O]_nCH_3$ are situated further downfield the closer is the group to the end of the chain, which indicates that terminal oxygen atoms have greater coordinating power (basicity). Analogous results have been obtained for glymes $CH_3O[CH_2CH_2O]_nCH_3$.

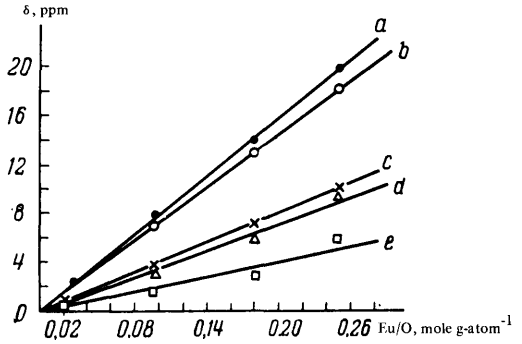


Figure 11. Dependence of shift (at 60 MHz) on ratio of Eu dpm$_3$ to oxygen for different groups in the compound $CH_3\overset{e}{O}CH_2\overset{d}{O}CH_2CH_2\overset{b}{O}CH_2\overset{a}{O}CH_2\overset{c}{C}H_2\overset{a}{O}CH_2\overset{b}{C}H_2\overset{d}{O}CH_2\overset{e}{O}CH_3$ dissolved in CCl_4 at room temperature [159].

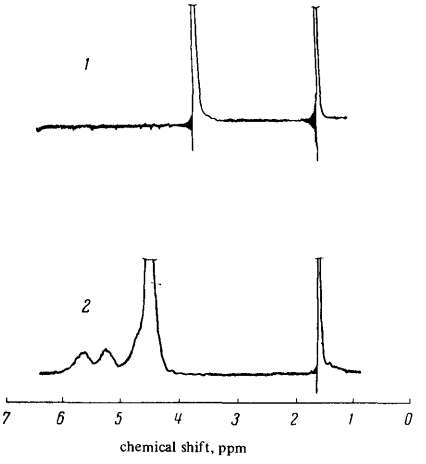


Figure 12. Nuclear magnetic resonance spectrum (60 MHz) of solution of polyethylene glycol PEG-400 in CCl_4 at room temperature: 1) in absence of shift reagent; 2) in presence of Eu dpm$_3$ with C_P/C_S = 0.4.

Use of a shift reagent facilitates determination of the molecular weights of polypropylene glycol [204] and polyethylene glycols [159] by means of the end-groups. Addition of the europium complex to a polyethylene glycol separates the signals due to terminal, penultimate, and central methylene groups (Fig. 12). The degree of polymerisation is calculated from the relative areas of the signals of terminal and central methylene groups. The resulting

molecular weights are close to the specified values (Table 11).

Table 11.

Mol. wt. from specification	400	600	1000
Mol. wt. from spectrum	370	550	986

8. Compounds with Spectra studied in the presence of Shift Reagents

Alcohols

Aliphatic [16,26,28,32,84,99,101,103,105,106,128,157,182,205-220].
Aromatic [35,69,214,221,222,223].
Cyclic [15,23,28,36,40,61,66,87,104,107,128,141,143,145,147,175,183,184,188,193,198,205,216,218,224-260].

Ketones

Aliphatic [33,100,106,110,161,219,220].
Aromatic [69,240,261].
Cyclic [66,89,97,110,126,127,132,160,176,189,191,196,197,215,229,232,235,237,239,240,250,252,262-274].

Ethers and esters [69,100,106,117,131,137,141,149,161,163,171,184,200,201,203,204,206,211,223,234,242,250,252,264,275-294].

Carbohydrates [23,31,203,259,290,295-300].

Other oxygen-containing compounds [20,21,32,33,97,110,112,118,140,160,192,198,218,240,263,267,281,289,292,301-310].

Amines

Aliphatic [20,26,32,99,105,125,220,303,311-313].
Aromatic [20,124,125,259,314].
Cyclic [20,82,148,315-319].

Nitrogen-containing heterocycles [20,48,69,70,84,92,109,119,140,144,150,164,173,194,238,267,268,301,305,317,320-326].

Amides [301,327-335].

Other nitrogen-containing compounds [117,142,220,301,336-339].

Sulphur-containing compounds [96,114,123,195,196,243,272,285,301,306,308,340-346].

Phosphorus-containing compounds [31,34,83,121,122,186,199,219,302,345,347].

Polymers [102,106,159,161,200,201-204,288,348].

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Shift reagents greatly increase the possibilities of nuclear magnetic resonance spectroscopy. In some cases the information obtainable from the n.m.r. spectrum determined at a frequency of 60 MHz in the presence of the europium shift reagent is greater than that provided by the spectrum at 220 MHz in the absence of a shift reagent [173]. It may be expected that the preparation of new shift reagents, in particular with a selective action towards certain functional groups and suitable for application in polar solvents, as well as detailed physicochemical investigation of reagent–substrate–solvent systems, will still further extend the range of application of this method.

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Formation and Dissociative Breakdown of Chlorophyll and Its Synthetic Analogues in Solution

B.D.Berezin and O.I.Koifman

A critical survey is made of studies on the mechanism, kinetics, and thermodynamics of the formation and the dissociation of chlorophyll, its metal analogues, and other metal porphyrins. Consideration is given mainly to results published during the past decade. Special attention is paid to complexes of the most important natural porphyrin—chlorophyllic acid. A list of 120 references is included.

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I. INTRODUCTION

Research on chlorophyll and structurally similar complexes of other porphyrins has entered a new stage during the past twenty years. The comprehensive study of the properties of this numerous group of complexes is progressing as one of the most important links in the chain of diverse problems waiting to be solved on the path to mastery and conscious control of photosynthesis. Until recently the most intensely studied physicochemical properties were the optical and electrophysical properties of chlorophyll, its analogues, and products of their reversible chemical reactions[1-20]. Many interesting results have been obtained by infrared[3-5,10,12,18,19], nuclear magnetic resonance, and electron spin resonance spectroscopy[4-6,12]. A special place is occupied by investigations on the electronic absorption spectra and spectral luminescent properties of chlorophyll, its structural analogues, and their photoreduced forms[1,4-11]. Scale investigations on the properties of photoreduced forms of chlorophyll and other porphyrin compounds, made in the Soviet Union by Krasnovskii, Evstigneev, and others[6,11,15-17,20], have formed the basis of fertile new insights into the rôle and nature of the transformations of the inner-complex pigment system in the photosynthesising apparatus of plants while functioning in the living cell.

Products of the dark reduction and the photoreduction of metal analogues and structural analogues of chlorophyll, as well as of the complexes formed by association with metal salts, have been widely studied during recent years[10,19,20]. Results of paramount importance have been obtained in this field. However, they are not directly connected with the subject of the present Review, and therefore will not be covered. Naturally, in view of what has been said, the Reviewers do not aim to give any complete list of references on these questions. Such a list can be found in the reviews cited above.

Experimental researches on the physicochemical properties of chlorophyll and other tetrapyrrole pigments during the past decade have been accompanied by quite fruitful theoretical investigations[21-29]. A critical survey of scientific results on the structure of these molecules obtained by spectroscopic methods and theoretical calculation will be found in the monograph by Gurinovich et al.[5]

Chlorophyll and other metal porphyrins utilise their coordinating properties in their formation and decomposition, as well as their functioning in vegetable and animal organisms, so that the investigation of these properties is of considerable interest. Although the first attempts at quantitative examination of the dissociation of chlorophylls-a and -b in solution were made more than thirty years ago[30-32], since then the formation of metal analogues of chlorophyll from metal salts and the corresponding "ready made" porphyrin molecules, as well as their dissociation, have been studied almost entirely qualitatively or at best semi-quantitatively. The results of these numerous attempts were summarised in Phillips' review[33]. Systematic studies of the formation and the decomposition of chlorophyll-like inner-complex compounds were begun about fifteen years ago. They can be regarded as originating with the appearance of papers by Kukhtevich[34,35], Caughey and Corwin[36], Fleischer[37], and one of the present Reviewers[38]. Within a short time numerous data were obtained on the coordination properties of chlorophyllic acid and other porphyrins, and on the mechanism of the formation and the decomposition of structural analogues† and metal analogues‡ of chlorophyll in various solvents. There is at present no review of the porphyrins in which due attention is paid to quantitative investigations of coordination properties.

The well known and extremely comprehensive and interesting monograph by Falk[8] discusses only out-of-date results of semi-quantitative kinetic investigations of the dissociation and formation of metal porphyrins, so that judgments and conclusions based on them are often unsound. The aim of the present paper is to examine critically research results on the coordination properties of porphyrins and to elucidate the main laws governing the formation and the breakdown of chlorophyll and other metal porphyrins in solution.

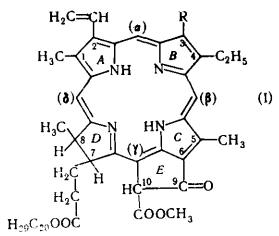
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† Structural analogues of chlorophyll are taken to be porphyrins and their derivatives of similar structure to chlorophyllic acid, i.e. most tetrapyrrole pigments with conjugation in the macro-ring.

‡ Metal analogues of chlorophyll are taken to be inner-complex compounds of metals with chlorophyllic acid other than the magnesium complex.

II. FORMATION OF METAL AND STRUCTURAL ANALOGUES OF CHLOROPHYLL IN SOLUTION

Most complexes of chlorophyllic acid (I), otherwise termed phaeophytin ($H_2\Phi$)



(I) R = CH_3; chlorophyllic-a acid; R = CHO; chlorophyllic-b acid

are formed by heating metal salts (MX_2) with phaeophytin dissolved in an organic solvent. The procedure suggested by Zalesky[39] has been widely used up to the present time. Glacial acetic acid (HOAc) is used as solvent, with a large excess of the metal acetate as the salt. The phaeophytin is complexed by heating the mixture on a boiling waterbath for 2 h. It has since been shown[40] that such treatment produces no changes in the phaeophytin molecule, and glacial acetic acid is one of the most favourable media[41] for the formation of metal analogues ($M\Phi$) of chlorophyll:

$$H_2\Phi + MX_2 \rightleftarrows M\Phi + 2HX. \quad (1)$$

Formation of $M\Phi$ takes place most rapidly in glacial acetic acid. Zalesky's method can be used to obtain stable copper(II), cobalt(II), nickel(II), iron(II), manganese(II), palladium(II), silver(II), and zinc(II) complexes. Organic solvents of other types—alcohols, esters, ethers, ketones, pyridine, quinoline, dimethylformamide—are used to prepare the cadmium(II), mercury(II), lead(II), silver(I), and certain other complexes, which are unstable even in weakly proton-donating media[41]. However, complexes of alkali and alkaline-earth metals (other than magnesium) cannot be obtained by this method, for reasons which will become clear from the subsequent discussion. Nor can treatment of the porphyrin with the metal alkoxide in alcohol or pyridine, generally adopted for other porphyrins[42], be used to prepare alkali-metal analogues of chlorophyll, owing to the instability of the cyclopentanone ring (E) of chlorophyllic acid in the presence of alkaline reagents[43]. Beryllium(II), calcium(II), strontium(II), and barium(II) analogues of chlorophyll also have not yet been prepared.

Chlorophyll itself, the progenitor of all metal phaeophytins, can be obtained by introducing magnesium into the phaeophytin molecule by means of a Grignard reagent[33,42] or a magnesium subhalide prepared from magnesium and iodine in dry pyridine[44]. Later results[45] seem to allow hope that the magnesium ion may be introduced directly into the phaeophytin molecule from solutions of its salts in organic solvents. The actual possibilities of this method will be discussed below. First we shall examine the formation of complexes from natural porphyrins—chlorophyllic-a acid.

1. Formation of Metal Analogues of Chlorophyll in Solution

The most detailed study has been made of the formation of complexes of chlorophyllic acid. The first attempt at a quantitative kinetic study of reaction (1) was made by Baker and Hodson[46], who measured the rates of formation of nickel phaeophytinate $Ni\Phi$ in methanol. They were able to obtain only empirical rate constants and an empirical kinetic equation of fractional order, which was attributed to unjustifiably severe experimental conditions and inaccurate measurements. These results were subjected to critical discussion by Berëzin and Sosnikova[38], who made a series of investigations[47-52] aimed at establishing the kinetics of the formation of metal analogues of chlorophyll in ethanol using the iron(II), cobalt(II), nickel(II), copper(II), zinc(II), silver(II), cadmium(II), mercury(II), and palladium(II) complexes as examples. Experiments were made with chlorophyllic acid under mild conditions between 15° and 50°C. The concentration of the metal salts was varied from 0.00025 M to 0.025 M. Reaction (1) took place in the presence of a considerable excess of the salt, since the concentration of phaeophytin-a did not exceed 0.000025 M. The reaction was of the first order with respect to salt concentration at all concentrations of copper(II) acetate, iron(II) chloride, and cobalt(II) chloride. With other metals the order with respect to salt concentration fell below unity as the concentration increased. The first order of reaction (1) with respect to phaeophytin was strictly maintained in ethanol with all the salts studied at all the temperatures. The general character of the kinetic dependence of reaction (1) on salt concentration is illustrated in Fig. 1 for the formation of cadmium(II) phaeophytinate[48]. Fig. 2 shows the typical dependence for most salts of the order of reaction (1) on salt concentration, illustrated by the formation of the cadmium complex from the acetate.

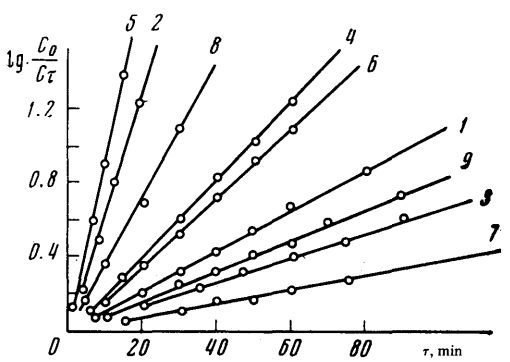


Figure 1. Rates of formation of cadmium phaeophytinate-a at different salt concentrations c and temperatures (°C): 1) 0.0025 M CdI_2 at 30°; 2) 0.0025 M CdI_2 at 40°; 3) 0.00025 M $Cd(NO_3)_2$ at 30°; 4) 0.00025 M $Cd(NO_3)_2$ at 40°; 5) 0.0025 M $Cd(NO_3)_2$ at 30°; 6) 0.0025 M $CdCl_2$ at 30°; 7) 0.00025 M $CdCl_2$ at 30°; 8) 0.0025 M $CdCl_2$ at 40°; 9) 0.00025 M $CdCl_2$ at 40°.

It was concluded from the results[38,48-50] that, at low concentrations of metal salts (below 0.0005 M), reaction (1) conforms to the second-order kinetic equation

$$-\frac{dc_{H_2\Phi}}{dt} = k_v \cdot c_{H_2\Phi} \cdot c_{MX_2}. \quad (2)$$

Values of k_V in Egn. (2) obtained at salt concentrations of 0.00025 M and below can be regarded as true rate constants. At higher concentrations k_V has smaller values, which are in some measure arbitrary (concentration rate constants).

Among the many causes of the "concentration" dependence of the rate constants discussed in the literature[53] two—the change in properties and structure of the solvent with increase in the salt concentration, and also the change in the geometrical configuration of the coordination sphere of the reactant salt with increase both in its own concentration and in that of a foreign electrolyte—must probably be regarded as the most significant. In several cases additional causes—association of the salts and also weak interaction between the salt and side-chains of the porphyrin—may no doubt operate[53]. The latter leads to "weighting" of the porphyrin molecule and changes the reactivity of its main coordination centre—the four cyclic nitrogen atoms.

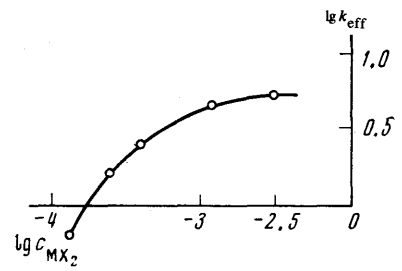


Figure 2. Concentration dependence of rate of formation of cadmium phaeophytinate.

Determinations[48-53] of the principal kinetic parameters for the formation of nine metal analogues of chlorophyll-a showed (Table 1) that "concentration" dependence of the rate constant is absent with certain salts, e.g. copper(II) acetate and cadmium(II) nitrate, iodide, and chloride; reaction (1) obeys the kinetic equation (2) at all concentrations of these salts. With other salts, e.g. cobalt(II) nitrate, the rate constant is almost independent of concentration. Finally, the "concentration" dependence is large with zinc(II) nitrate, cadmium(II) acetate, and nickel(II) nitrate. Such specific behaviour of different salts is explained by differences in the stability of particular coordination structures of the salts in organic solvents. Table 1 shows that, under comparable conditions, the rate of reaction (1) depends little on the electronic structure, charge, or radius of the cation.

The mean rate constant of reaction (1) for salts of eight metals is $(9.8 \pm 6.4) \times 10^2$ M^{-1} h^{-1}.

The rate of formation of the nickel complex is around 10%, and that of cobalt phaeophytinate around 1%, of the average for the remaining complexes. The activation energy is more sensitive to the nature of the cation than is the rate, and varies from 10.6 kcal for copper(II) acetate to 31 kcal for cobalt(II) chloride. In conformity with the kinetic compensation effect, which is strictly observed[54] in the series of metal phaeophytinates, the entropy of activation varies correspondingly from −26 to +30 e.u. for the above salts. The rate of formation of phaeophytinates depends substantially on the anionic composition of the medium[48-52]. In the case of the cadmium and cobalt salts the reaction velocity diminishes[53] in the sequence of anions $NO_3^- > Cl^- > CH_3COO^-$ (Table 1). The instability constants of the cadmium and cobalt salts with these anions decrease in the same sequence: i.e. the stability of the M–X bond in solution increases. The nature of the bond between the anion X^- and the cation probably has an indirect effect on the stability of the solvent sheath of the salt MX_2Solv_{n-2}§, determining the rate and other kinetic parameters of reaction (1). The effect of the structure of the coordination sphere in the initial salt on the formation of metal analogues of chlorophyll has been studied[50,51] by measuring the rate of formation of copper phaeophytinate at various temperatures with various complex salts of copper—malonate, succinate, citrate, and alaninate—in 90% ethanol and in ammoniacal–ethanolic media, in which the above salts have satisfactory solubility. Inspection of the experimental results (Table 2) indicates that replacing the anion X^- in the coordination sphere of the salt MX_2 changes the reaction velocity not more than tenfold, independently of the type of coordination (linear, cyclic, or inner-complex) of the organic anion as ligand, of the stability of its bond with the cation. Alanine and citrate form very stable chelate complexes with the Cu^{2+} ion[55], yet they react with chlorophyllic acid just as easily as does copper acetate. From these facts it may be concluded that reaction (1) takes place with the undissociated salt MX_2, and the stage of activation of the salt involves loss of a solvent molecule—not of an anion—from the coordination sphere of the cation.

Table 1. Kinetic parameters of the formation of metal analogues of chlorophyll

$$H_2\Phi + MX_2 \rightarrow M\Phi + 2HX$$

in ethanol at 25°C.

Metal salt	Rate constant $10^{-2}k_v$, M^{-1} h^{-1}	Activation energy, kcal $mole^{-1}$	Entropy of activation, e.u.
$FeCl_2$	4.48±0.23*	13.8±1	−16±3
$CoCl_2$	0.018±0.002**	31.0	+30
$Cu(OAc)_2$	0.011±0.001*	23.9	+6.1
$Co(NO_3)_2$	0.106±0.012*	24.0	+11
	0.068±0.008**	18.0	−10.5
$Ni(NO_3)_2$	0.34±0.04*	15.5	−15.4
	1.42±0.28***	23.6	+14.4
$Cu(OAc)_2$	59.1±0.6	10.6±1.2	−26±4.0
$Cu(NO_3)_2$	91.3±5.5*	12.9±1.2	−13±3.0
$Zn(NO_3)_2$	2.30±0.20*	14.1±0.5	−16.2±1.6
	15.0±2.0***	14.1±0.7	−12.5±2.0
$Cd(OAc)_2$	15.1±1.2***	13.4±1.5	−15±5.0
	3.37±0.08*	16.5±0.7	−7.5±2.5
$Cd(NO_3)_2$	26.0±1.7	16.2±0.2	−4.5±0.7
CdI_2	5.25±0.40	19.6±1.7	+4±7.0
$CdCl_2$	18.5±0.8	11.1±0.5	−22±2.0
HgI_2	23.0±3*	13.4±2	−14±7.0
$HgCl_2$	21.9±2.4*	—	—
$AgNO_3$	2.66±0.15*	19.0±0.2	+34±0.5
$PdCl_2$	4.76±0.15*	18.0±1	−2±3.0

*Concentration of salt 0.0025 M.
**Concentration of salt 0.025 M.
***Concentration of salt 0.00025 M.

Saturation of 90% ethanol with ammonia (Table 2) lowers the rate of reaction (1) by factors of 10–20, with increase in the energy and the entropy of activation, which was explained[50] both by rearrangement of the inner coordination sphere of the Cu^{2+} ion from a solvate to an ammine and by rearrangement of the solvent structure around this

§ Solv = solvent molecule; n = maximum coordination number of cation under specific conditions.

sphere. The high energies and entropies of activation in aqueous–alcoholic and ammoniacal–alcoholic media were explained by the formation of a second and subsequent solvation spheres in the vicinity of coordinated water or ammonia, which is impossible in the case of alcohols.

Table 2. Formation of copper phaeophytinate from various complex copper salts in ethanol at 25°C.

Cu salt	$10^{-3}k_v$, M^{-1} h^{-1}	E, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.	Ethanol
$Cu(OAc)_2$	5.91	10.6	−26	Absolute
$Cu(NO_3)_2$	4.67 *	41.7	+82	90%
$Cu(NO_3)_2$	0.445 *	42.5	+80	90% + NH_3
Cu(Malonate)	1.23 **	13.2	−16	90%
Cu(Malonate)	0.0273 **	41.8	+73	90% + NH_3
Cu(Succinate)	0.150 **	28.4	+31	90% + NH_3
Cu(Citrate)	0.390 **	21.9	+11	absolute
Cu(Alanine)	2.06 **	6.5	−37	90%

*Concentration of salt CuX_2 is 0.0025 M.
**Salt concentration 0.00025 M.

Table 3. Kinetic parameters of formation of mercury(II) phaeophytinate at 25°C.

Salt	Concn., 10^3c, M	$10^{-3}k_v$, M^{-1} h^{-1}	E, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.	Solvent
$HgCl_2$	0.25	28.0	13.9	−5	ethanol
$HgCl_4^{2-}$	0.25	very slow	—	—	ethanol
$HgCl_2$	0.25	0.58	56.4	+101	methanol
$HgCl_2$	0.50	0.43	48.7	+129	methanol
$HgCl_4^{2-}$	0.25	0.67	12.7	−16	methanol
$HgCl_4^{2-}$	2.50	0.046	11.3	−26	methanol
HgI_2	2.50	0.230	13.4	−14	ethanol
HgI_4^{2-}	2.50	very slow	—	—	ethanol
HgI_2	2.50	0.021	13.1	−22	methanol
HgI_4^{2-}	0.25	0.068	21.8	+14	methanol

The kinetics of reaction (1) with chloride and iodide complexes of mercury was studied in order to determine the effect of the number of coordination sites of the cation occupied by simple anions[51]. Table 3 shows that decrease in the number of solvent molecules located in the coordination sphere of Hg^{2+}, from two for HgX_2 to zero for HgX_4^{2-}, strongly inhibits reaction (1) in ethanol, whereas in methanol $Hg\Phi$ is formed at the same rate from $HgCl_2$ and $HgCl_4^{2-}$, and the rate from HgI_4^{2-} is even higher than from HgI_2. An explanation for such unusual behaviour of mercury salts will be given in discussing the mechanism of reaction (1) in later sections.

Here, however, we must note the extraordinarily strong dependence of the rate of formation of phaeophytinates on the nature of the solvent. This becomes obvious when it is remembered that the solvent forms the structure of the coordination sphere of the salt MX_mSolv_{n-m}, and determines the strength of the M–X and M–Solv bonds in solution, as well as the degree of solvation of the reactants: i.e. it determines the energy and entropy components of the free energy of activation of reaction (1). Berëzin and Smirnova[41,56–62] measured the rates of this reaction with copper(II) and zinc(II) salts in various types of organic solvents—alcohols, ketones, ethers, amides, nitrogen-containing heterocycles, and aliphatic acids—and found a thousandfold variation in the rate of formation of metal analogues of chlorophyll depending on the nature of the solvent (Table 4). The rate is maximal in glacial acetic acid, and minimal in pyridine. The effect of the solvent on the kinetics of reaction (1) was explained[56–62] by variation in the stability of the solvent coordination sphere of the salt MX_2Solv_{n-2}, i.e. in ease of rupture of the M–Solv bond, and by spatial factors, in particular steric hindrance by solvent molecules in the coordination sphere of the activated salt impeding entry of the large flat phaeophytin molecule.

Table 4. Kinetic parameters of the reaction

$$Cu(OAc)_2 + H_2\Phi \rightarrow Cu\Phi + 2HAc$$

in various solvents at 25°C.

Solvent	$10^3c^0_{Cu(OAc)_2}$, M	10^3k_v, M^{-1} h^{-1}	E, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.
C_2H_5OH	0.130	5.91	10.6	−26
CH_3OH	0.150	29.7	14.8	− 4
n-$C_5H_{11}OH$	0.240	1.99	27.1	31
$(CH_3)_2CO$	0.280	3.26	11.1	−16
$O(CH_2—CH_2)_2O$	0.300	0.165	17.2	− 6
CH_3COOH	0.160	95.0	11.2	−14
$HCON(CH_3)_2$	0.900	0.131	18.9	− 2
C_5H_5N	0.900	0.0331	22.9	9
C_6H_7N	0.900	0.101	24.1	15

Table 5. Kinetics of formation of copper phaeophytinate in ethanol–glycerol media at 25°C.

Glycerol / ethanol	Viscosity (discharge time)	$10^{-3}k_v$, M^{-1} h^{-1}	E, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.
0:100	4 s	3.42	10.6	22.7
20:80	10 s	1.81	10.8	23.4
50:50	1 min	1.46	11.9	20.0
80:20	7 min	0.44	12.8	19.4

Table 4 indicates that the reaction velocity of (1) decreases and the activation energy increases with increase in the volume occupied by the solvent in the immediate vicinity of the cation[63,64]. This is characteristic of dioxan, pyridine, quinoline, dimethylformamide, and n-pentanol. It is significant that merely strengthening the coordinate link (ethanol → methanol) does not diminish the rate, although it increases the activation energy appreciably. Another extremely interesting aspect is that change in the state of phaeophytin molecule $H_2\Phi$ has hardly any effect on the reaction velocity. Thus in glacial acetic acid, which forms a strong hydrogen bond with nitrogen atoms in the reaction centre of phaeophytin, the rate exceeds that in ethanol by a factor of 15; the latter solvent slightly blocks the nitrogen atoms. Interaction of π–π type between the aromatic rings of phaeophytin and nitrogen heterocycles (pyridine, quinoline) also has no appreciable effect on the reactivity of phaeophytin. Thus the rates of (1) in quinoline and in dimethylformamide are roughly the same. An analogous effect of nature of solvent on reactivity was established with phaeophytin and zinc salts[41,56–61]. Neither the displacement of the keto–enol equilibrium of phaeophytin-a occurring in ethanol–glycerol

solutions nor the increase in viscosity of the medium (Table 5) has a significant effect on the rate of reaction (1).[62] It was suggested that the enolic form nevertheless possesses a higher kinetic coordinating power than does the ketonic form.

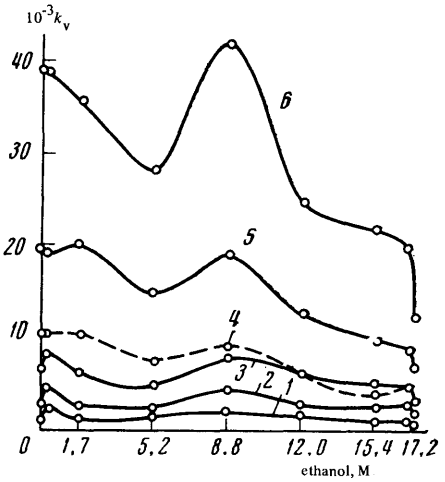


Figure 3. Dependence of rate constant of formation of CuΦ on composition of ethanolic acetic acid for different approximate $Cu(OAc)_2$ concentrations (M) at different temperatures (°C): 1) 0.0025 at 15°; 2) 0.0025 at 25°; 3) 0.0025 at 35°; 4) 0.00025 at 15°; 5) 0.00025 at 25°; 6) 0.00025 at 35°.

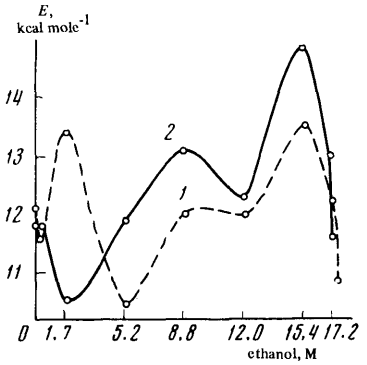


Figure 4. Dependence of activation energy of CuΦ on composition of solvent for different approximate concentrations (M) of $Cu(OAc)_2$: 1) 0.0025; 2) 0.00025.

Berëzin and Klopova[65-67] found several extremal points n the variation of rate, activation energy, and entropy of ıctivation of reaction (1) with solvent composition in ethanoic acetic acid (Figs. 3–5). The extrema were attributed[66] o resolvation, on passing from acetic acid to alcoholic nedia, of the solvate complex $[M(OAc)_2(HOAc)_{n-2}]$ through $M(OAc)_2(HOAc)_{n-2-m}(C_2H_5OH)_m]$ to $[M(OAc)_2(C_2H_5OH)_{n-2}]$; hey were attributed also to formation of an association complex $CH_3COOH...C_2H_5OH$ with a stable hydrogen bond; and in some measure to resolvation of the reaction centre of phaeophytin from >N...HOCOCH₃ to >N...HOC₂H₅ and >NH...O(H)–C₂H₅. Rearrangement of the structure of the pure solvent produced by small additions of another solvent, in particular stabilisation of the structure of methanol, is probably quite an important factor[68].

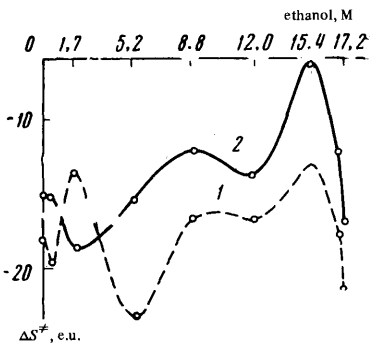


Figure 5. Dependence of entropy of CuΦ on composition of solvent for different approximate concentrations (M) of $Cu(OAc)_2$: 1) 0.0025; 2) 0.00025.

Phillips and others[69] found that the nature of the solvent had a very strong effect on the rate of formation of other metal porphyrins. Cobalt(II) salts react rapidly with porphyrins in dry acetone even at 25°C. Addition of a small quantity of water greatly retards the reaction. A still more interesting observation, which cannot yet be interpreted, was made on nickel salts: nickel(II) reacts very rapidly when the reaction is conducted in higher alcohols (butanol, pentanol) or in phenol, but very slowly in methanol, ethanol, or water. The reasons for such behaviour are now being studied in detail on complexes of cobalt(II) with chlorophyllic acid[70].

2. Formation of Complex Compounds—Structural Analogues of Chlorophyll

Quantitative investigation of the formation of porphyrin complexes—structural analogues of chlorophyll—began comparatively recently[71]. The need for their study arose from the importance and great biological activity not only of chlorophyll but also of other metal porphyrins, possessing a different system of side-chains and different central metal atoms. The selective action of metal porphyrins is probably governed precisely by the nature and range of substituents. These change the σ- and π-acceptor and the donor properties of the conjugated macrocycle, as well as the ability of the central metal atom to coordinate additional ligands involved in particular biological acts (photosynthesis, respiration, oxidation, decomposition, etc.). It is therefore a very urgent task to investigate kinetic and equilibrium aspects of the formation of metal porphyrins as a function of the nature and number of side-chains in porphin.

Choi, Fleischer, et al.[71,72] studied complex formation by αβγδ-tetrapyridylporphin (H_2TPP) with copper(II), cobalt(II), manganese(II), and nickel(II) salts in glacial and aqueous

acetic acid. This porphin possesses good solubility in proton-donating solvents, including aqueous media. The reaction, probably represented by the equation

$$H_2TPP + M^{2+}_{Solv} \xrightarrow{k_v} MTPP + 2H^+_{Solv} \quad (3)$$

has the first order with respect both to the porphin and to the metal. Unfortunately, the reaction velocity was measured only at a single concentration (~ 0.004 M) of the metal salt, and the unjustified assumption was made that copper(II) acetate is present in glacial acetic acid as Cu^{2+}. Calculation based on the second-order equation (2) gave for the rate constants of reaction (3) involving copper, cobalt, manganese, and nickel diacetates the respective values 1400, 310, 210, and 87 M^{-1} h^{-1} at 25°. The reaction takes place considerably more slowly than with chlorophyllic acid (cf. Table 4).

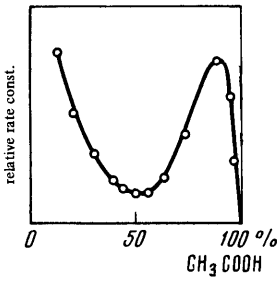


Figure 6. Dependence of rate of formation of CuTPP on acetic-acid concentration.

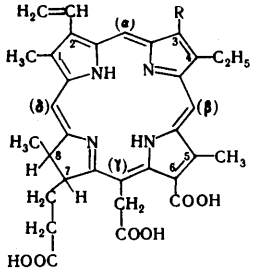
The formation (3) of copper and zinc complexes from the perchlorates in 8.3% aqueous acetic acid containing 0.01 M perchloric acid has rate constants at 25°C of 63 and 22 M^{-1} h^{-1}. Replacement of acetic acid by water molecules in the coordination sphere lowers the rate by 50–67%. The rate of reaction (1) in aqueous solution is inversely proportional[71,72] to the hydrogen-ion concentration, but in aqueous acetic acid it passes through a maximum in the 90% acid (Fig. 6). However, these facts were left unexplained[71]. It may be supposed that protonation of the pyridine residues accelerates the reaction (in concentrated aqueous acetic acid) owing to increased protonation of the pyrrole nitrogen–hydrogen bonds, while protonation of the reaction centre, i.e. of the pyrrole nitrogen atoms (aqueous perchloric acid) lowers the reaction velocity. Competition between the two processes may produce the observed variation (Fig. 6). The fact that cadmium, lead, and mercury complexes of tetrapyridylporphin are not formed under the given conditions[71] causes no surprise, since these complexes are unstable in proton-donating media.

Brisbin and Balanura[73] studied the kinetics of the reaction between manganese(II) and haematoporphyrin in glacial acetic acid, and suggested a reaction mechanism which was subjected to an impartial critique[74]. The effect of the pH of the medium on the rate of coordination of sulphonated deuteroporphyrin IX by Cu^{2+} ions was studied by Weaver and Hambright[75]; and the catalytic action of nitrogen-containing solvents on the reaction of zinc(II) with water-soluble porphyrins was investigated by Stein and Plane[76]. We shall not discuss these papers, since their results introduce nothing significantly novel into the kinetics and the mechanism of the reactions of metal salts with porphyrins.

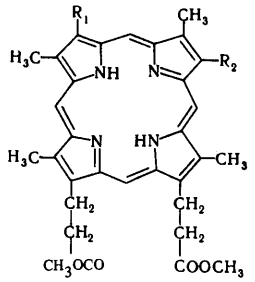
A most interesting paper by Baum and Plane[77] deals with the direct introduction of magnesium into a porphyrin from a solution of a salt in an ordinary organic solvent (acetone, methanol). The rate of incorporation of magnesium into the dimethyl ester of deuteroporphyrin IX is given by the kinetic equation

$$\frac{d[MP]}{dt} = k_1\frac{[PH_2]}{[H^+]} + k_2\frac{[PH_2][Mg^{2+}][Py]}{[H^+]} \quad (4)$$

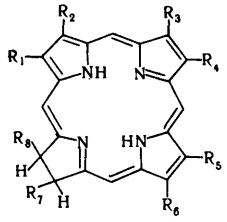
in which the rate constants of the uncatalysed reaction and of the reaction catalysed by pyridine or other nitrogen-containing solvent are respectively $k_1 = 4.7 \times 10^{-4}$ and $k_2 = 3.6$ M^{-1} h^{-1}, the corresponding activation energies being $E_1 = 36.5$ and $E_2 = 15.8$ kcal $mole^{-1}$. Comparison with Table 1 indicates that the rate of coordination of magnesium by porphyrins from solution is vanishingly small, but the catalytic effect of nitrogen-containing compounds is so intense that the rate of incorporation of magnesium approaches those for cobalt from the dichloride and the diacetate in ethanolic solution. These results encourage the hope of the direct introduction of magnesium into chlorophyllic acid, and also a fresh look at the formation of chlorophyll in the living cell[78].



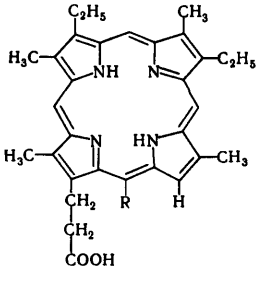
(II) chlorin-e_6 R = CH_3
(III) rhodin-g_7 R = CHO



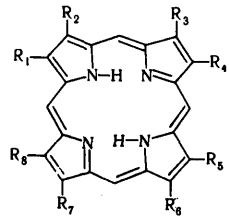
(IV) mesoporphyrin IX: dme: $R_1 = R_2 = C_2H_5$
(V) protoporphyrin IX: dme: $R_1 = R_2 = CH = CH_2$



(VI) chlorin:
$R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = R_7 = R_8 = H$
(VII) acetiochlorin II:
$R_1 = R_4 = R_5 = R_8 = CH_3$
$R_2 = R_3 = R_6 = R_7 = C_2H_5$



(VIII) pyrroporphyrin XV: R = H
(IX) phylloporphyrin XV: R = CH_3



(X) porphin:
$R_1 = R_2 = R_3 = R_4 = R_5 = R_6 = R_7 = R_8 = H$
(XI) acetioporphorin I:
$R_1 = R_3 = R_5 = R_7 = CH_3$; $R_2 = R_4 = R_6 = R_8 = C_2H_5$
(XII) aetioporphorin II:
$R_1 = R_4 = R_5 = R_8 = CH_3$; $R_2 = R_3 = R_6 = R_7 = C_2H_5$

Berëzin and Koifman have reported[79-86] systematic investigations of the effect of structural units of the porphyrin molecule on the kinetics of the formation of metal porphyrins (see Table 6). To facilitate discussion of the results we give here the structural formulae of the natural and synthetic porphyrins investigated. Opening the cyclopentanone ring (ring E in structure I), i.e. the conversion of phaeophorbide-a into chlorin-e_6 (II), doubles the reaction velocity, while the activation energy and entropy remain almost unchanged. The explanation given[80] was that the substitution of carboxyl for -CO.R at $C_{(6)}$ in chlorin-e_6 changes the inductive effect exerted by the substituent on the nitrogen atoms of the macrocycle. The carboxy-group, while possessing about the same conjugation effect as the group it replaces, probably exerts a greater inductive effect, so that the nitrogen–hydrogen bond in the chlorin may become strongly protonated, with a tendency to accelerate the reaction

$$H_2P + MX_2 \rightarrow MP + 2HX. \qquad (5)$$

The suggestion that the state of the nitrogen–hydrogen bond in porphin greatly influences the coordinating power of the compound is supported[79] by a comparison of chlorophyllic-a and -b acids (structure I). Conversion of $H_2\Phi$-a into $H_2\Phi$-b is accompanied by a decrease in the rate of coordination of the Cu^{2+} ion roughly to one-seventh, with an appreciable increase in activation energy, associated with an increase in electron density on the nitrogen–hydrogen bond under the influence of the positive conjugation effect (+*C*-effect) of the 3-formyl group (structure I). The greater stability of chlorophyll-b in solution finally provides convincing evidence that the above hypothesis[74,79] is correct. An adverse effect of the 3-formyl group on the rate of formation of complexes in solution has been established also in a comparison[81] of chlorin-e_6 (II) with rhodin-g_7 (III), which have the same structural relationship as chlorophyllic-a and -b acids.

Table 6. Kinetic parameters of formation of copper complexes of natural and synthetic porphyrins in ethanol at 25°C.

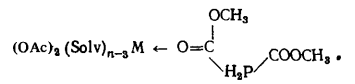
Porphyrin	$10^4 c^0_{Cu(OAc)_2}$, M	$10^{-3}k_{eff}$, $M^{-1}\,h^{-1}$	*E*, kcal mole^{-1}	$\Delta S^{\neq}$; e.u.
Chlorophyllic-a acid	3.75	5.91	11.8	−17
Chlorophyllic-b acid	4.50	0.18	14.0	−17
Phaeophorbide-a	3.75	4.75	7.5	−28
Chlorin-e_6	4.50	8.20	6.5	−34
Rhodin-g_7	2.70	1.70	6.4	−38
Synthetic chlorin	5.50	2.20	11.2	−21
Porphin	4.45	2.00	13.2	−16
Mesoporphyrin IX dme*	2.50	6.70	7.5	−31
Protoporphyrin IX dme*	2.50	3.60	8.8	−29
Pyrroporphyrin XV	2.64	15.50	7.0	−32
Phylloporphyrin XV	0.90	48.50	10.0	−18
Aetioporphyrin I	2.30	7.00	13.4	−12
Aetioporphyrin II	2.30	6.90	12.8	−14
Aetiochlorin II	2.30	7.50	11.3	−18

*dme = dimethyl ester.

The conversion of chlorin-e_6 (II) into mesoporphyrin (IV), involving disappearance of one carboxyl conjugated with the macro-ring at $C_{(6)}$, and of the 2-vinyl group, produces hardly any change in the kinetic parameters[84] (Table 6). Here similar electron-accepting substituents (COOH and $CH:CH_2$) have been replaced by similar alkyl and "pseudo-alkyl" substituents (C_2H_5 and $CH_2.CH_2.COOH$). The rate constants remain unchanged probably because the 2- and 6-substituents have opposite effects.

Protoporphyrin coordinates copper salts at half the rate observed with mesoporphyrin[84]. Conversion of the latter (IV) into the former (V) involves replacement of the two alkyl substituents at $C_{(2)}$ and $C_{(4)}$ by vinyl groups, which possess an analogous but weaker +*C*-effect than that of the formyl group. This leads to a diminution in the protonation of the nitrogen–hydrogen bond and a lower reaction velocity.

Completely unexpected results were obtained[82] for the coordinating properties of porphin (X) and synthetic chlorin (VI), and their comparison with the aetioporphyrins (XI) and (XII).[85] Porphin and synthetic chlorin do not differ in the kinetic parameters of coordination (Table 6). Hence the hydrogenation of one "semi-isolated" double bond of a pyrrole ring has no appreciable effect on the state of the N–H bond and the reactivity of the macro-ring. Nevertheless, porphin and synthetic chlorin coordinate copper salts at one-quarter the rate observed with chlorin-e_6 or mesoporphyrin. The favourable effect of residues of propionic acid was explained[84] by primary coordination of the metal salt on them:



Because of favourable arrangement of methoxycarbonyl groups relative to the main coordinating centre (the four nitrogen atoms of the macrocycle), primary coordination probably favours the enclosure of both reaction centres in a solvent "cage", which will increase the rate and lower the activation energy. The entropy of activation will also diminish in conformity with the compensation effect characteristic[74,83] of reaction (5). The aetioporphyrins (XI) and (XII), in which the propionic-acid residues have been replaced by alkyl groups, possess double the activation energy with the same rates of coordination. A similar result appears on comparing aetiochlorin (VII) with chlorin-e_6 (II). The high rates of reaction (5) with aetioporphyrin and aetiochlorin, relative to those with porphin (X) and chlorin (VI), are explained by the presence of a factor counterbalancing the energy factor in the coordination of porphyrins[85]. This factor is universal solvation, which is probably less favourable to alkylated than to unsubstituted pyrrole rings in porphyrins. The solvation factor is especially strongly developed when the symmetry of the porphyrin molecule and also that of the π-electron system of the macro-ring are destroyed. Pyrroporphyrin XV (VIII), which contains no 6-substituent, coordinates at double the rate observed with mesoporphyrin (Table 6). Finally, phylloporphyrin XV (IX), which unlike pyrroporphyrin has a γ-alkyl group, exhibits the maximum rate of coordination of metal salts[86]: its rate of reaction with copper(II) acetate exceeds that of phaeophytin-b by a factor of 270.

Falk's monograph[8] gives the relative rates of formation of copper(II) complexes with mesoporphyrin, protoporphyrin, and 2,4-diacetyldeuteroporphyrin in aqueous solutions of sodium dodecyl sulphate as 7 : 1.5 : 1.0. These agree well with the above results[78-85], and support the main conclusions reached.

Thus by now not only has the strong effect of structural features of the porphyrin molecule on its coordinating reactivity been established but the influence of energetic factors (variation in state of nitrogen–hydrogen bond produced by substituents), solvation factors, and primary coordination on the kinetic parameters has also been shown.

All the conclusions reached[79-85] for reaction (5) with copper(II) salts have been found to hold also for zinc(II) salts[74].

3. Mechanism of Formation of Metal Analogues of Chlorophyll and Other Metal Porphyrins

The formation of complex compounds with large planar molecules having continuous peripheral conjugation exhibits several features distinguishing such reactions from the formation of complexes (often termed ligand substitution) with simple ligands[87,88]. Several factors are responsible for such distinguishing features: (i) the ligand possesses low mobility in solution, and is a target for the more mobile reactant—the salt molecule (or ions); (ii) the ligands are acidic, and are usually extremely difficult to convert to the anionic state ($H_2P \rightarrow 2H^+ + P^{2-}$); (iii) the continuous π-cloud of the conjugated macrocyclic system (structures I–XII) shields the reaction centre of the ligand, including the four inner nitrogen atoms; and (iv) solvation of the ligand involves complicated phenomena, as the ligand carries multifarious centres of solvation.

The main feature of the formation of metal porphyrins is its slowness in comparison with the coordination of other ligands. Systematic investigations of the formation of metal analogues of chlorophyll[48-51,56-62] indicated, for organic solvents possessing no appreciable ionising power, the stoichiometric equation

$$M(Solv)_{n-m}X_m + H_2\Phi(Solv)_p \rightarrow M\Phi(Solv)_q + 2HX(Solv)_s + (n-m+p-q-2s)\,Solv \quad (6)$$

which conforms to the second-order kinetic equation (2).

Reaction (6) probably takes place in a single stage in most of the solvents studied, since intermediate compounds were not detected, either kinetically or spectroscopically[48,49]. In several cases, however, formation of an intermediate complex of type $H_2\Phi.MX_2$ was a possibility[57,89,90]. Such complexes are formed in glacial acetic acid when reaction (6) is conducted with zinc(II) chloride, cobalt(II) chloride, cobalt(II) acetate, iron(II) chloride, palladium(II) chloride, and mercury(II) acetate in ethanol. They are distinguished from a phaeophytinate by a hypsochromic shift of the first two bands and a strong bathochromic shift of the other three bands in the electronic absorption spectrum. An exception is $H_2\Phi.Hg(OAc)_2$.[91] The intermediate complexes are far less stable than complexes of the bivalent metal with pyridine and with alcohols. They are converted into the corresponding phaeophytinates either at room temperature ($H_2\Phi.Co(OAc)_2$) or when the solutions are boiled ($H_2\Phi.FeCl_2$).

The stoichiometric mechanism (using Langford and Gray's classification[87]) of the formation of metal porphyrins is most probably covered by two possibilities (written here in simplified form)—(*a*) in a single bimolecular stage

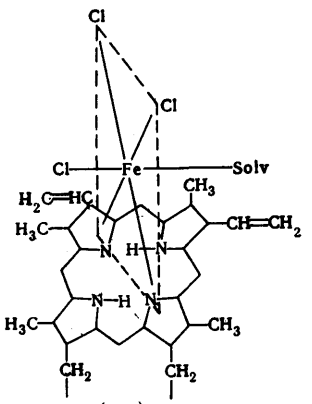
$$H_2P + MX_2 \rightarrow [MX_2 \cdot H_2P]^{\ddagger} \rightarrow MP + 2HX \quad (6a)$$

(*b*) in two stages with preliminary formation of an intermediate

$$H_2P + MX_2 \underset{\text{(stage I)}}{\overset{\text{rapid}}{\rightleftharpoons}} MX_2 \cdot H_2P \xrightarrow[\text{(stage II)}]{\text{slow}} [MX_2 \cdot H_2P]^{\ddagger} \rightarrow MP + 2HX. \quad (6b)$$

The two reaction paths undoubtedly cross different forms of potential barrier, but the shape and height of the final peak in the potential curve, determined by the structure of the transition state $[MX_2.H_2P]\dagger\dagger$, are the same, since the latter has the same structure in reactions (6a) and (6b). According to existing schemes of classification[86,88,92,93] the stoichiometric mechanism of reactions (6a) can be regarded either as associative bimolecular S_E2[93] or as a concerted process with associative activation[87]. The mechanism of reactions (6b) can be denoted dissociative unimolecular S_E1 in Ingold's classification[92].

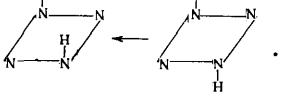
It is of interest to examine data on the detailed mechanism of the elementary stage of the coordination of porphyrins by metal salts. These data also deepen and refine information on the stoichiometric mechanism. It was first established[37] that the dimethyl ester of protoporphyrin in acetone, chloroform, and other weakly solvating solvents forms with iron(II), iron(III), cobalt(II), platinum(IV), tin(II), and zinc(II) salts initially a complex whose spectrum is closely similar to that of the diprotonated porphyrin $H_2PH_2^{2+}$. On this basis the structure



(XIII)

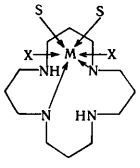
was assigned to the complex, and is probably closest to reality. This structure is supported by the results of infrared spectroscopy[37]: the vibrations of the nitrogen–hydrogen bond were shown to change in character.

In strongly solvating media, such as water, alcohols, pyridine, etc., the above cations gave metal porphyrins without forming intermediates. No intermediate complexes are formed when the cations Ni^{2+}, Cu^{2+}, Hg^{2+}, and Cd^{2+} react with the dimethyl ester of protoporphyrin in acetone. In the reaction with chlorophyllic acid the formation of intermediate complexes was only rarely observed in polar solvents, including acetone[57,89,90]. Such complexes are generally produced in glacial acetic acid, since the metal–solvent bond in the solvate coordination spheres of the salt MX_2Solv_{n-2} is not very stable. It follows from these observations that the elementary act, both in reactions (6a) and in stage (I) of reactions (6b), involves the detachment of one or two solvent molecules from the inner sphere of the salt, i.e. its activation to MX_2Solv_{n-3} or MX_2Solv_{n-4} and activation of the porphyrin, which evidently entails conversion of the *trans*-form of H_2P into the *cis*-form and its partial resolvation[50]:



The reacting system (6a) forms an activated complex (transition state $[H_2P.MX_2]\dagger\dagger$), but the reacting system (6b) forms a complex of type $H_2P.MX_2$. There is no

special reason to doubt that these two structures are the same (XIV).



(XIV)

The reacting system (6a), having reached the summit of the potential barrier, readily splits off $2H^+$, $2X^-$, and perhaps some of the solvent molecules from the inner sphere to give the metal porphyrin (MP). The reactant system (6b) remains in the potential well at the summit of the barrier, since detachment of the anions X^- and perhaps also H^+ is difficult in a weakly solvating medium, in which alone are intermediates formed. Addition of a more polar solvent leads to the displacement of H_2P molecules from the intermediate complex, and the reacting system (6b) returns to the initial state. This indicates that the intermediate is a very unstable complex. In spite of this, the second stage of reaction (6b) is difficult and is accomplished only on prolonged heating. The reason is that, as had been suggested[90], the formation of metal porphyrins in this case involves breakdown of the intermediate complex into the starting materials, which react by scheme (6a).

Thus it is highly probable[90] that metal porphyrins are not formed at all by scheme (6b). This view is supported by the analogous behaviour of the MX_2-H_2P system in strongly proton-donating solvents, in which the species $H_2PH_2^{2+}$ is formed, resembling the intermediate $H_2P.MX_2$ in properties. The rate constant for the formation of CuΦ in 95% formic acid at 25°C (6.5 M^{-1} h^{-1}) is 0.03% of its value in glacial acetic acid. The activation energy has increased from 10.5 to 29 kcal: i.e. it includes the activation energy for the breakdown of $H_2PH_2^{2+}$ to H_2P and the energy of activation of MX_2 and H_2P in reaction (6a).

Falk in his monograph[8], on the basis of results obtained by Phillips et al.,[69] concludes that the formation of metal porphyrins, like that of complexes of chlorophyllic acid, occurs predominantly by scheme (6a): i.e. it has a bimolecular mechanism¶. Some interesting results were obtained[94,95] on the detailed mechanism of reaction (6): complex formation between copper(II) and mesoporphyrin is accelerated by the presence of hydroxyquinoline (OX^-) at a concentration corresponding to formation of $CuOX^+$, after which the rate drops sharply when $Cu(OX)_2$ is formed. Thus a chelating ligand added to the MX_2-H_2P system may act either as an activator or as an inhibitor. The authors[94,95] were unable to give the true reasons for such behaviour of foreign ligands. The conclusion is suggested by data[48-51,56-62] on the complexes of chlorophyllic acid (Tables 2–4). When the reactant salt MX_2Solv_{n-2} contains the anion X^- in the inner sphere, as occurs with hydroxyquinoline, the number of coordinated solvent molecules diminishes from 4 to 0, and their bonding with the cation becomes weaker. This weakening favours the reaction, increasing the rate and lowering the activation energy. Decrease in the number of solvent molecules in the inner sphere acts in the opposite direction, and when $n - 2 = 0$ reaction may cease, as in the case of $Cu(OX)_2$.[94,95] The above considerations readily explain facts established by one of us[48-53,56-62]—that reaction (6) is not retarded by such chelating additives as malonate, succinate, citrate, and alanine (Table 2), which occupy no more than 2–4 coordination sites in the inner sphere of Cu^{2+}, leaving 2 solvent molecules in it; that reaction (6) occurs at very high rates with the very stable complex salts $HgCl_2$ and HgI_2 (Table 3); and that rates are lower in solvents having bulky molecules, such as dioxan, pentanol, dimethylformamide, pyridine, etc. (Table 4).

Nevertheless, the formation of metal porphyrins with $HgCl_4^{2-}$ and HgI_4^{2-} and the absence of reaction[53,63,64] with $[Co(NH_3)_6]^{3+}$, $[CoCl(NH_3)_5]^{2+}$, $[Co(HCOO)_2(NH_3)_4]^+$, $[Fe(CN)_6]^{4-}$, and $[Fe(CN)_5NO]^{2-}$ salts indicate a second possible detailed mechanism for reaction (6a)—displacement of ligands from their positions in the course of interaction between the porphyrin and the complex salt[51]—which is possible with HgX_4^{2-} but impossible with $[CoL_6]^{n+}$ and $[FeA_6]^{n-}$. Porphyrins can react by this mechanism with salts containing no solvent molecules in the inner sphere, provided that such salts can be distorted with contraction of the coordination sphere and the freeing of two sites for the development of interaction with two nitrogen atoms in the reaction centre of the porphyrin.

Investigation of the coordination of porphyrins (6) raises the question whether the kinetic parameters will be affected if reaction occurs with the cation of the dissociated salt:

$$M^{2+} + H_2P \rightarrow MP + 2H^+ \qquad (7)$$

a form in which the stoichiometric equation has been written[8,33,35,37]. Such a crude representation of the reaction suggests that the salt MX_2Solv_{n-2} is completely or almost completely dissociated, and is present either in the form $MSolv_n^{2+} + 2X^-$ or else as the ion-pair $[MSolv_n]X_2$. Such a state of the salt is possible with strongly solvating solvents only when weak M–X coordination interaction is present in solution (MX_2 has a high instability constant). All the results obtained for the coordination of chlorophyllic acid indicate that the kinetic parameters are little affected by change in state of the salt from $[MX_2Solv_{n-2}]$ to $[MSolv_n]X_2$ or even to $[MSolv_n]^{2+} + 2X^-$. This conclusion is based on experiment and is easily explained by the reaction mechanism (6a).

In order to understand the detailed mechanism it is necessary to know how the state of the porphyrin molecule—in particular that of the N–H bond—changes during activation. Several results tending to answer this question will be found in Refs. 50, 79, and 86. In organic solvents porphyrin undergoes the elementary act as H_2P, not as $H_2PH_2^{2+}$, PH^-, or P^{2-}.[50,90] The slight dependence of the rate of reaction (1) on the nature of the salt cation under identical experimental conditions indicates that the major component of the total activation energy resides in the stretching of the N–H bond. Investigation of the effect of structural changes in the porphyrin molecule[79-86] on the rate and on the energy and entropy of activation of reaction (6) has not only confirmed this conclusion but also established that polarisation (protonation) of the N–H bond favours the reaction.

III. DISSOCIATION OF CHLOROPHYLL, ITS METAL ANALOGUES, AND OTHER METAL PORPHYRINS IN SOLUTION

In this Section we shall discuss the heterolytic breakdown or solvolytic dissociation of porphyrin complexes,

¶ These authors[8,69] write the mechanism S_N2, not S_E2: i.e. they take porphyrin to be the reagent, which on the above considerations cannot be regarded as reasonable.

which occurs only in proton-donating media. Dissociation of the complexes into ions

$$MP + mn\,Solv \rightleftarrows M(Solv)_n^{2+} + P^{2-}(Solv)_m \quad (8)$$

is not observed owing to the very slight acidity of H_2P and the very great stability of metal–porphyrin complexes MP in solution. Appreciable dissociation begins to develop in media containing solvated protons H^+_{Solv} or molecules of strong acids. It occurs as protolytic dissociation

$$MP + 2H^+_{Solv} + 2X^- \rightleftarrows MX_2 + H_2P \quad (9)$$

but in media of high acidity

$$MP + 4H^+_{Solv} + 2X^- \rightleftarrows MX_{2(Solv)} + H_2PH^{2+}_{2(Solv)}. \quad (9a)$$

1. Dissociation of Chlorophyll and its Labile Metal Analogues

The first attempt at a quantitative kinetic study of the dissociation of chlorophyll was made by Mackinney and Joslin[30-32], who examined the reaction

$$Mg\Phi + 2HX \rightarrow Mg^{2+} + H_2\Phi + 2X^- \quad (9b)$$

in 90% aqueous acetone, using oxalic, sulphurous, sulphuric, and hydrochloric acids. The reaction was presumably of the first order with respect to the acid, but the order with respect to chlorophyll was not established, and no reliable kinetic characteristics were obtained. The failure of these experiments is explained by the choice of an unsuitable proton-donating solvent, in which partial protonation of $H_2\Phi$ to $H_2\Phi H_2^{2+}$, aggregation of $H_2\Phi$, etc. were possible. An important result[30-32] was that chlorophyll-a dissociates seven times as rapidly as chlorophyll-b†.

The kinetic experiments on the dissociation of chlorophyll and its derivatives have since been repeated by Schanderl et al.,[96] who used 80% aqueous acetone with additions of 10^{-4} M hydrochloric acid. Under the given conditions chlorophyll-a was found to dissociate more rapidly than chlorophyll-b by a factor of 5.5, while the activation energy was the same at 10.5 kcal mole^{-1}. Replacement of the phytyl residue ($C_{20}H_{39}$) in the chlorophylls by ethyl, methyl, and hydrogen, i.e. conversion of the chlorophylls into the ethylphaeophorbides, methylphaeophorbides, and phaeophorbides, produces slight acceleration of dissociation (the experimental rate constants for the a-compounds at 25°C are respectively 0.0103, 0.0127, 0.0156, and 0.0171 min^{-1}) without affecting the activation energy. The investigations provided no information on the mechanism of reaction (9) or the nature of the bond between magnesium and the porphyrin. The dissociation of chlorophyll and its analogues has therefore been studied under comparable conditions by Berëzin and Drobysheva[89,91,97-105]. The dissociation of chlorophyll-a and of cadmium and mercury phaeophytinates was examined[102] in absolute ethanol with small additions of glacial acetic acid, between 20° and 60°C. The results[102] are given in Table 7.

The dissociation of chlorophyll in ethanolic acetic acid occurs irreversibly in conformity with Eqn. (9), is strictly of the first order with respect to chlorophyll, has the activation energy $E = 13.7 \pm 0.5$ kcal mole^{-1} and the entropy of activation $\Delta S\dagger\dagger = -37 \pm 1$ e.u., and is very strongly dependent on (varies more rapidly than the fourth power of) the total concentration of acetic acid. Dissociation of the cadmium analogue of chlorophyll is reversible and of the first order with respect to the complex, with zero activation energy. Fig. 7 illustrates the dependence of the effective dissociation rate constants of chlorophyll and its cadmium analogue on the square of the total acetic-acid concentration. Dissociation of the cadmium complex is of the second order with respect to acetic acid and of the fourth order with respect to the solvated proton, whose concentration is calculated on the assumption that it is the attacking species in the act of dissociation of the complex.

† Chlorophyll-b is the magnesium complex of chlorophyllic-b acid—see structure (I).

Table 7. Dissociation of Mg, Cd, and Hg phaeophytinates in ethanolic acetic acid.

Complex	HOAc in ethanol, M	Temp., °C	k_{eff}, h^{-1}	Complex	HOAc in ethanol, M	Temp., °C	k_{eff}, h^{-1}
MgΦ	2.0	25	0.013*	CdΦ	0.02	25	0.68
		40	0.038			35	0.64
		50	0.076			45	0.62
		60	0.142		0.04	25	1.86
	4.0	25	0.34		0.06	25	3.80
	8.0	25	3.30		0.10	25	13.8
	10.0	25	41.5		0.20	25	83.0
				HgΦ	0.02	25	very rapid

*Calculated by means of the Arrhenius equation.

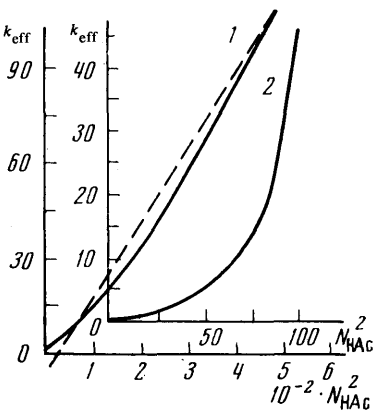


Figure 7. Dependence of effective dissociation rate constant on acidity of medium for: 1) CdΦ; 2) MgΦ.

The explanation offered[91,102] for such an unusual dependence was that not only $C_2H_5OH_2^+$ but also others, in particular CH_3COOH, may function as active protogenic species with not too stable metal porphyrins (the magnesium, cadmium, and mercury(II) complexes). Probably changes in the structure and properties of the solvent (ethanol) with increasing concentration of acetic acid should also be taken into account. These changes may have a large kinetic effect[65-67]. Since the nature of the reagent species in the act of dissociation of chlorophyll and its analogues is an important question, efforts must be directed to finding a proton-donating solvent in which one type of proton-donor would predominate, and its concentration could be calculated exactly. The Reviewers are making a search for such media in the laboratory.

Table 7 indicates an unusually large variation in the kinetic stability of the magnesium, cadmium, and mercury complexes. The mercury complex HgΦ is surprisingly unstable: in the presence of traces of acetic acid in ethanol it dissociates instantaneously. The cadmium complex is several orders of magnitude more stable. Chlorophyll is the most stable among these labile phaeophytinates. This stability is a not unimportant factor in Nature's choice as the principal complex for effecting photosynthesis.

2. Dissociation of Stable Complexes of Chlorophyllic Acid and Other Porphyrins

The stability of porphyrin complexes is of great interest for biochemistry, so that qualitative observations of this most important property were made long ago, and the results have been summarised[8,33,36]. The first quantitative data on the rates of dissociation of copper aetioporphyrin (XII) were published by Caughey and Corwin[36]. The dissociation was studied in glacial acetic acid with additions of sulphuric acid monohydrate. The results are given in Table 8.

Table 8. Rates of dissociation of copper aetioporphyrin at 30°C.

H_2SO_4, M	H_0	Expt. rate constant $10^{-6}k_{obs}$, h^{-1}
0.216	−2.02	0.715
0.267	−2.13	2.05
0.287	−2.17	2.83
0.312	−1 22	4.41
0.328	−0.328	5.00

The reaction velocity is described by the kinetic equation[36]

$$-\frac{d[\mathrm{CuAeP}]}{dt} = k\,[\mathrm{CuAeP}]^2 \cdot h_0^4 . \qquad (10)$$

The interpretation of the results[36] was subsequently criticised[37,108,107], and has not found support in investigations on other porphyrins.

Table 9. Kinetic parameters of dissociation of MΦ-a in glacial acetic acid at 25°C.

Complex	Added H_2SO_4, mole	E, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.	k_{eff}, h^{-1}
AcOFeΦ	0.500	17.30	−29	$8.95\cdot10^{-4}$
NiΦ	0.500	16.50	−28	$1.20\cdot10^{-3}$
	1.00	17.00	−26	$1.67\cdot10^{-3}$
CuΦ	0.200	16.40	−28	$1.23\cdot10^{-3}$
	0.500	15.30	−31	$1.92\cdot10^{-3}$
PdΦ	1.00	17.10	−29	$2.18\cdot10^{-3}$
CoΦ		12.80	−44	$1.61\cdot10^{-3}$
NiΦ		27.40	−11	$1.3\cdot10^{-6}$
CuΦ		19.00	−29	$9.8\cdot10^{-5}$
ZnΦ		10.10	−40	0.976
AgΦ		19.60	−16	$2.25\cdot10^{-3}$

Rates of dissociation of stable complexes of chlorophyllic acid (a-series) have been measured[97–103] by a spectrophotometric method. The iron(III),[80] nickel(II),[100] copper(II),[97,100] and palladium(II)[100] complexes dissociate at a measurable rate in strongly proton-donating media (sulphuric acid monohydrate in glacial acetic acid), but the zinc(II),[98] cobalt(II),[89] and silver(II)[101] complexes are decomposed even in weakly proton-donating media (glacial acetic acid and its mixtures with ethanol). At high temperatures the rates of dissociation of the nickel and copper complexes could also be measured in glacial acetic acid. The phaeophytinates-a of iron, zinc, and silver, like those of magnesium, cadmium, and mercury, dissociate according to Eqn. (9) or (9a). Dissociation of the copper, palladium, nickel, and cobalt phaeophytinates-a is accompanied by degradation of the phaeophytin molecule $H_2\Phi$-a to slightly coloured products. It was assumed[97] that detachment of the metal ion may yield an active form of the $H_2\Phi$-a molecule, which breaks down rapidly:

$$\mathrm{M\Phi} + 2\mathrm{HAc} \xrightarrow[\text{slow}]{} \mathrm{H_2\Phi^*} + \mathrm{MAc_2}\,, \qquad (11)$$

$$\mathrm{H_2\Phi^*} \xrightarrow[\text{rapid}]{} n\,\mathrm{A}\,. \qquad (12)$$

Reaction (12) involves no change in the side-chains, but a fundamental breakdown of conjugation occurs in the macrocycle, which is impossible without preliminary detachment of the metal by reaction (11) and freeing of the reaction centre. Conditions for the mechanism of dissociation by processes (11) and (12) are at present under investigation[105]. It is favoured by a strong metal–nitrogen covalent bond in the dissociating complex, except in the iron(III) complex[91]. The occurrence of reactions according to scheme (9) or (11) and (12) depends greatly on the temperature and on the solvent. Figs. 8 and 9 illustrate the variation in the absorption spectra[91] for these reactions.

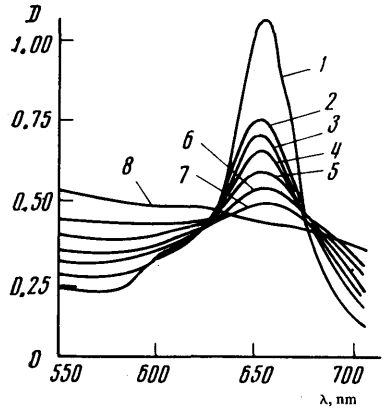


Figure 8. Dissociation of CuΦ in glacial HOAc + 0.5 M H_2SO_4 at 70°C (l = 1 cm): 1) initial CuΦ in acid mixture at 25°C; 2) initial CuΦ under experimental conditions; and after different periods of time (h): 3) 0.25; 4) 0.75; 5) 1.25; 6) 2.25; 7) 3.25; 8) 5.0.

Table 9 lists the kinetic parameters of dissociation for the stable complexes of phaeophytin-a.[91,100,108] Dissociation of stable complexes of chlorophyllic-a acid is very slow, with mean activation energies of 10–12 kcal (with the exception of the nickel complex in glacial acetic acid) and strongly negative entropies of activation, caused by the

high polarity of the transition state and the active participation of the solvent in the act of dissociation. Tables 7 and 9 indicate that the sequence of kinetic stability is

$$AcOFe\Phi \rhd Pd\Phi > Ni\Phi > Cu\Phi > Co\Phi > Ag\Phi > Zn\Phi \gg Mg\Phi > Cd\Phi > Hg\Phi.$$

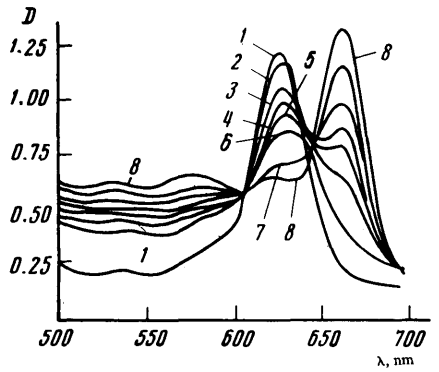


Figure 9. Dissociation of AcOFeΦ in mixture of glacial HOAc + 1.0 M H_2SO_4 at 50°C (l = 1 cm): 1) initial complex in glacial acetic acid; 2) complex under experimental conditions; and after different intervals of time (h): 3) 1; 4) 2; 5) 3; 6) 5; 7) 10; 8) 20.

Interesting investigations have recently been made[104] on the kinetic and the thermodynamic stability of complexes of chlorophyllic-b acid with copper and zinc. Table 10 compares the kinetic stability of metal analogues of chlorophyll-a and -b. The rates of dissociation of complexes of chlorophyllic-b acid are lower than those of the a-derivatives by factors of 25–300, and their rates of formation are also lower by factors of 10–10^2. These differences are attributed[104] to the influence of the formyl group in changing the electron density on the nitrogen atoms of the reaction centre. The retarding effect of this group on the rates of formation and dissociation of the complexes is eliminated in the equilibrium constants. Therefore the a- and b-complexes differ only threefold in thermodynamic stability.

Table 10. Dissociation of complexes of chlorophyllic acid in glacial acetic acid.

Complex	k_{eff}, h^{-1}	E, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.	K_{eq}
CuΦ-b	$0.38\cdot10^{-5}$	23.4	−25	$1.6\cdot10^{-9}$
CuΦ-a	$9.8\cdot10^{-5}$	19.0	−29	$5.1\cdot10^{-9}$
ZnΦ-b	$3.1\cdot10^{-3}$	10.9	−49	$2.4\cdot10^{-5}$
ZnΦ-a	0.976	10.1	−40	$7.3\cdot10^{-5}$

Iron(III) protoporphyrin (haemin) and the corresponding complex of chlorophyllic-a acid show similar kinetic stability in glacial acetic acid with additions of sulphuric acid (cf. Tables 9 and 11).

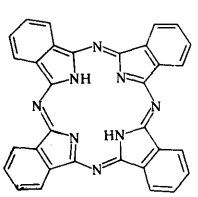
3. Mechanism of the Dissociation of Metal Porphyrins in Proton-donating Media

The first hypotheses on the mechanism of the protolytic dissociation of metal porphyrins were put forward in Ref. 36. The kinetic equation (10), showing the second order with respect to the porphyrin, was interpreted on the assumption of the improbable transition state $(MP.2H^+)_2$††. A combination of two porphyrin molecules in true solution, in which the relatively immobile "target" aetioporphyrin molecules, having no active peripheral substituents, are attacked by a proton-donating species, can hardly be taken seriously. The improbability of such a mechanism has been pointed out[97,107]. The first order of the reaction with respect to the porphyrin has since been shown convincingly[97–102,104] for the dissociation of complexes of chlorophyllic acids and also of iron protoporphyrin[105]. It follows from this that the transition state contains one molecule of the porphyrin complex.

Table 11. Dissociation of iron(III) protoporphyrin (haemin) in glacial acetic acid.

Added H_2SO_4	Temp., °C	k_{eff}, h^{-1}	E, kcal mole^{-1}	$\Delta S^{\neq}$, e.u.
2.0	25	0.00177		
2.0	70	0.056		
2.0	80	0.103	15.9	−34
2.0	90	0.200		
5.0	25	0.00845		
5.0	60	0.205		
5.0	70	0.455		
5.0	80	1.04	18.0	−24
5.0	90	1.88		

The general applicability of this principle to all complexes of tetrapyrrole ligands is supported by kinetic data on the dissociation of phthalocyanine complexes. Phthalocyanine



(XV)

is a close structural analogue of the porphyrins, and is widely used as a simple model thereof[1,3–10,14–16,110]. The complexes (MPc) dissociate in conformity with the third-order kinetic equation

$$\frac{dc_{MPc}}{dt} = -k \cdot c_{MPc} c^2_{H_3O^+}. \qquad (13)$$

Several facts have shown convincingly[109] that a termolecular mechanism is most probable. In concentrated sulphuric acid, in which a metal phthalocyanine generally dissociates at a measurable rate only at 100°C, the attacking species is not H_2SO_4 but H_3O^+. In the transition state $[MPc.2H_3O^+]$†† are two N–H bonds resulting from acid–base interaction, two coordinate links $M \leftarrow OH_3^+$ appear, and two M←N bonds are deformed and become weaker. The mechanism of dissociation can be represented by the scheme

$$MPcH^+ + H^+_{Solv} \underset{I}{\overset{k_1}{\rightleftarrows}} HN \cdots \overset{\overset{N}{\downarrow}}{\underset{Solv\ N}{M}} \leftarrow N + H^+_{Solv} \underset{II}{\overset{k_2}{\rightleftarrows}} HN \cdots \overset{\overset{Solv\ N}{\searrow\downarrow}}{\underset{N\quad Solv}{M}} \cdots NH \xrightarrow{\overset{H^+_{Solv}}{k_3}} H_2PcH^+ + M^{2+}_{Solv}. \qquad (14)$$

With stable phthalocyanines processes I and II take place in a single stage.

The close structural analogy between phthalocyanine and porphyrins suggested[100,110] that mechanism (14) applied also to stable complexes of the latter. Experimental examination of the kinetic order of the dissociation of stable complexes of chlorophyllic acid with respect to the proton-donating species has not yet given general support to this hypothesis. An unambiguous result has so far been obtained[89] only for iron(III) phaeophytinate, whose rate of dissociation in glacial acetic acid is proportional to the total concentration of sulphuric acid. In weakly ionising media such as acetic acid we have $[H_2SO_4]_{total} \simeq [H^+_{Solv}]$, which confirms the validity of Eqn. (13) for AcFeΦ and of the mechanism (14).

On the basis of the general theoretical concepts of coordination chemistry it may be predicted that it will be sufficient to break one M–N bond and convert it into M⁺...NH in the case of labile metal phthalocyanines and metal porphyrins, in which the metal–ligand bond is predominantly ionic. After the metal has been displaced from the plane of the macrocycle, subsequent rupture of the remaining bonds and transition to the structure (XIV) will take place readily. For these complexes we may not only expect the first order with respect to $[H^+_{Solv}]$ but also postulate the H_2SO_4 molecule and even HOAc as active protogenic species. This makes it clear why labile complexes dissociate instantly on the addition of traces of sulphuric acid to their acetic-acid solutions and show a high order with respect to the total concentration of acetic acid[91,100,102]. Chlorophyll itself can be included in this category: it is assumed that $k_1 \gg k_2$ in process (14).

IV. THERMODYNAMIC AND PHOTOCHEMICAL STABILITY OF CHLOROPHYLL AND ITS METAL ANALOGUES IN SOLUTION

The first paper on the thermodynamic stability of the zinc complex of the dimethyl ester of mesoporphyrin (ZnMP) appeared in 1961.[111] The instability constant in aqueous hexadecyltrimethylammonium bromide was found to be 10^{-29}. In conformity with critical comments[112] this value must be regarded as a very crude approximation. In spite of this, however, it clearly demonstrates the extraordinary stability of porphyrin complexes. In fact, zinc complexes with an instability constant of 10^{-16} are formed by one of the most strongly chelating ligands, ethylenediaminetetra-acetate[55]. Such great stability of porphyrin complexes is due to their very low rates of formation and dissociation, resulting from π-electron shielding of the four nitrogen atoms constituting the coordination centre. The first investigations in this field were made by Kukhtevich on the equilibrium formation of metal analogues of chlorophyll using an extraction method[34,35,113,114]. He studied the formation equilibria

$$M^{2+}_w + H_2\Phi_{org} \rightleftarrows M\Phi_{org} + 2H^+_w \qquad (15)$$

of bivalent zinc, cadmium, copper, and cobalt phaeophytinates by then partitioning them between the aqueous phase and an organic solvent (butanol). Kukhtevich calculated the equilibrium constants of (15) and the so called "extraction" constants

$$\frac{[M^{2+}]_w[\Phi^{2-}]_w}{[M\Phi]_{org}} = K_{M\Phi\,org/w} \qquad (16)$$

obtaining values of 2×10^{-23}, 5.2×10^{-20}, 5×10^{-20}, and 1.7×10^{-11} for CuΦ, CoΦ, ZnΦ, and CdΦ respectively. Complexes of chlorophyllic-a and -b acids had identical constants.

Kukhtevich also reported[35] so called "extraction" constants for both stages of the acid ionisation of phaeophytin:

$$K_1 = \frac{[H^+]_w \cdot [\Phi H^-]_w}{[H_2\Phi]_{org}} = 2.3 \cdot 10^{-11},$$

$$K_{1,2} = \frac{[H^+]^2_w \cdot [\Phi^{2-}]_w}{[H_2\Phi]_{org}} = 10^{-20}.$$

Data on the dissociation of phaeophytin differ sharply from the preliminary results reported by McEwen[115] for aetioporphyrin ($K_1 \simeq 10^{-16}$ and $K_{1,2} \simeq 10^{-32}$). Ionisation constants differing by a factor of 10^{12} cannot be explained in terms of molecular structure. The exact values of the acid dissociation constants of porphyrins, which are necessary for calculating the instability constants of their complexes, remain unknown, and their determination is an urgent problem in the physical chemistry of porphyrins. "Extraction" constants give only a crude indication of the order of stability of porphyrin complexes. However, these constants have correctly revealed the very great stability of the complexes, the great difference between the zinc and cadmium complexes in this respect, and the feebly developed acidic properties of chlorophyllic acid. Significant defects of the extraction method have been pointed out[116], and mention made of our ignorance of existing extraction equilibria and the absence of clarity concerning the mechanism of complex formation in a two-layer system comprising water and an organic solvent.

The difficulties associated with the direct measurement of equilibria involving porphyrin complexes led to the successful use[91,108,112] of two forms of kinetic method. The first procedure entailed calculating equilibrium constants for metal porphyrins (MP) from their known dissociation and formation rate constants obtained under identical conditions (temperature, solvent, anionic composition of the medium, etc.). The principle of detailed balancing was used[108], according to which the formation and dissociation stages of these compounds have the same transition state (Sections II and III). Dissociation equilibrium constants were found in this way for zinc, cobalt, copper, and nickel phaeophytinates in glacial acetic acid[91]. The second variant of the kinetic method was used to calculate dissociation equilibrium constants for the palladium(II), iron(II), and silver(II) phaeophytinates, since their formation rate constants could not be obtained under conditions of dissociation. This utilises the slight dependence of the formation rate constants of MΦ on the nature of the metal, i.e. that k_v^{form} is almost constant. We can then write the relation

$$\frac{K^0_{MP}}{K'_{M'P}} = \frac{k^0_v}{k'_v} \qquad (17)$$

for a complex adopted as standard and for the *i*th complex MP to be compared with it. If the equilibrium constant for the standard K^0_{MP} is taken to be unity, the relative equilibrium constant of M'P will be the ratio of the dissociation rate constants of the *i*th complex and the standard under comparable conditions:

$$K^i_{M'P} = k^i_v/k^0_v. \qquad (18)$$

Equilibrium constants were found in this way for the palladium(II), iron(III), and silver(II) complexes relative to copper(II) phaeophytinate as standard. The known true equilibrium constant of the standard enabled true constants to be obtained for PdΦ, AcOFeΦ, and AgΦ. Values obtained by both forms of the kinetic method are given in Table 12.[91]

The very great difference in stability between zinc and cadmium phaeophytinates makes it impossible to determine

their equilibrium constants in the same proton-donating medium. The constants of the cadmium complex were measured in ethanol with small additions of acetic acid, and those of the zinc complex in glacial acetic acid with small additions of ethanol. The results were then extrapolated to 50% ethanolic acetic acid. The rough values thus obtained were $K_{eq}^{Cd\Phi} \simeq 0.5$ and $K_{eq}^{Zn\Phi} \simeq 5 \times 10^{-7}$. Thus under identical conditions the complexes $Cd\Phi$ and $Zn\Phi$ would differ in stability by factors of about 10^6. Published data enable a crude estimate to be made of the dissociation equilibrium constant of chlorophyll—from the dissociation rate constant of chlorophyll measured[102] in ethanol containing 2 M acetic acid, and from the formation rate constant of magnesium mesoporphyrin, converted by means of the data in Tables 4 and 6 into the formation rate constant of chlorophyll in ethanol $k_v^{form} = 3.6 \times 10^{-5}$ M^{-1} h^{-1}—as

$$K_{eq} \approx \frac{0.013}{3.6 \cdot 10^{-6}} \approx 360$$

in ethanol–acetic acid medium. An analogous estimate of the equilibrium constant in 10 M ethanolic acetic acid yields 1.2×10^6, which exceeds the constant for zinc phaeophytinate by a factor of 10^{12}, and that for the cadmium complex by more than 10^6.

Table 12. Equilibrium constants for the dissociation of stable phaeophytinates in glacial acetic acid at 25°C.

Complex	$K_{eq} = \frac{[MOAc_2]}{[HOAc]^2} \cdot \frac{[H_2\Phi]}{[M\Phi]}$
$Zn\Phi$	$7.32 \cdot 10^{-5}$
$Co\Phi$	10^{-5}
$Ag\Phi$	$2.3 \cdot 10^{-7}$
$Ni\Phi$	$3 \cdot 10^{-8}$
$Cu\Phi$	10^{-9}
$Pd\Phi$	$8 \cdot 10^{-11}$
$AcOFe\Phi$	$5 \cdot 10^{-11}$

Several conclusions follow from the above values. Firstly, the positions of metal analogues of chlorophyll in the kinetic stability sequence (see above) and in the thermodynamic stability sequence

$$AcOFe\Phi > Pd\Phi > Cu\Phi > Ni\Phi > Ag\Phi > Co\Phi > Zn\Phi > Cd\Phi > Mg\Phi,\ Hg\Phi$$

do not coincide in those cases in which the rates of formation exhibit anomalies. The rate of formation of chlorophyll ($Mg\Phi$) exceeds those of its metal analogues by factors of 10^7–10^8. Therefore, while possessing far higher kinetic stability than cadmium phaeophytinate, chlorophyll is markedly inferior in thermodynamic stability. Certain anomalies in the rates of formation of the nickel complex make it thermodynamically less stable than the copper complex, although the kinetic stability of the former is rather greater. The same applies to cobalt(II) and silver(II) phaeophytinates: the former is kinetically the more stable, whereas the silver complex exhibits the greater thermodynamic stability. In this connection, the numerous attempts to make deductions as to thermodynamic stability from the rates of dissociation of porphyrin complexes, which have been widely undertaken both abroad[8,33,36] and in the Soviet Union[112], must be regarded as a first, very rough approximation.

Secondly, the position of a complex in the kinetic stability sequence is determined predominantly by the covalency of the metal–porphyrin bond. Kinetic stability in solution is probably a quite reliable criterion of the type of bond. The magnesium–porphyrin bond is far more covalent than the corresponding bonds with cadmium and mercury(II). This covalency is responsible for the adequate stability of chlorophyll in the plant cell. Nevertheless, chlorophyll is far less covalent than the zinc complex, one of the least stable members of the group of stable phaeophytinates. This intermediate position of chlorophyll in the covalency sequence ensures that the magnesium shall carry a sufficient effective charge to favour coordination of the various molecules forming part of the complicated photosynthetic apparatus[2].

Thirdly, the position of a metal porphyrin in the thermodynamic stability sequence is largely determined by specific aspects of its formation in solution. Consideration of the mechanism and the kinetic parameters of the formation of metal porphyrins (Section II) shows that the stability (covalency) of the complex makes no significant contribution to its rate of formation. For this reason the thermodynamic stability sequence of metal porphyrins does not reflect their covalency.

The only serious rivals to metal porphyrins in their extraordinary stability are the phthalocyanine complexes[108]. Under very severe conditions (concentrated sulphuric acid) stable metal phthalocyanines dissociate at vanishingly low rates; metal porphyrins eliminate the cation instantly under these conditions. Such a substantial difference in stability between these close structural analogues has been explained by differences in the molecular structures of the ligands[110,117,118], by differences in their electron-donating and electron-accepting powers. It must be added that probably the most significant reasons why metal porphyrins are less stable than metal phthalocyanines are some departure of the molecules from planarity[8] and the absence from the molecular periphery of nitrogen atoms, which buffer the electron density in antibonding π-orbitals of the macrocycle. Coordination of a metal with phthalocyanine removes four pairs of electrons from such orbitals of the ligand. The resulting deficiency of π-electron density is immediately filled by the lone pairs of the outer nitrogen atoms[119]. Such a possibility is not available to a porphyrin molecule.

An important problem in the chemistry of porphyrin complexes is their photochemical stability in solution and its relation to their kinetic and thermodynamic stability. The lack of work in this field is acutely felt at the present time. A parallelism between photochemical and thermodynamic stability of phaeophytin complexes was reported[120] on the basis of qualitative and semi-quantitative experiments. The general conclusion was reached that phaeophytinates of the b-series are more resistant to fading than are those of the a-series.

Detailed quantitative investigations of the photochemical stability of chlorophylls-a and -b, chlorophyllic acids, and their complexes in ethanol and glacial acetic acid[99] have enabled these conclusions to be refined. Rate constants calculated for photochemical degradation over the range 20–60°C showed that the rate is little influenced by temperature but is strongly affected by the solvent. Photochemical fading is more rapid in acetic acid than in ethanol. However, the opposite effect is observed with cadmium phaeophytinate. Phaeophytins-a and -b have the same rates of fading in ethanol; cadmium phaeophytinate-a is twice as fast to light as the b-complex. In glacial acetic acid phaeophytin-b is four times as fast as phaeophytin-a.

No correlation between photochemical and thermodynamic stability is observed in either solvent. Thus in ethanol mercury(II) phaeophytinate is more stable to light than the zinc complex, whereas the magnesium and cadmium complexes are equally fast. In glacial acetic acid cobalt(II) phaeophytinate is more stable than the palladium and copper complexes. The sequence of diminishing photochemical stability in glacial acetic acid was found[99] to be

$$AcOFe\Phi > Ni\Phi > Co\Phi > Pd\Phi > Cu\Phi.$$

This sequence does not correspond to those of kinetic and thermodynamic stability. The lack of parallelism between light fastness and resistance to ionic dissociation is not unexpected, since there is no similarity in the mechanisms of the two processes[99].

Summing up the above account, we must note an acute lack of data on several aspects, despite the substantial progress made during the past decade in investigating the conditions and mechanism of the formation and decomposition of chlorophyll and its structural analogues. This applies primarily to the fine mechanism of dissociation of the complexes and directly to measurement of the formation equilibria of metal porphyrins. The main efforts of research workers in such an important and interesting branch of chemistry should be directed to solving these problems.

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Ivanovo Institute of Chemical Technology

U.D.C. 547.-585

Syntheses of Tetracarboxylic Acids

B.I.Zapadinskii, B.I.Liogon'kii, and A.A.Berlin

A systematic and general account of the literature data on the methods of synthesising tetracarboxylic acids capable of forming internal cyclic dianhydrides is given for the first time in the present review. These products have found extensive applications as starting materials for the synthesis of heterocyclic polymers, dyes, plasticisers, hardening agents for epoxy-resins, etc. Particular attention has been devoted to methods of synthesising aromatic tetracarboxylic acids and also products of greatest practical importance.
The bibliography includes 214 references

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I. INTRODUCTION

Only 10–15 years ago tetracarboxylic acids did not have practical applications although many of them had been isolated from the oxidation products of organic compounds or in the identification of diene systems by the Diels–Alder reaction. However, the situation changed radically when it became known that tetracarboxylic acids and their functional derivatives can be used as starting materials for the synthesis of thermostable products [polyimides [1] and poly(aroylenebisbenzimidazoles) [2]], plasticisers, antioxidants [3], hardening agents for epoxy-resins [4], etc. In addition, aroyleneimidazole dyes have again roused interest in recent years [5]. A systematic and general account of data on the methods of synthesising tetracarboxylic acids has therefore become necessary.

The present review deals with the methods of synthesis of only those tetracarboxylic acids whose derivatives are capable of intramolecular cyclisation. This limitation was imposed because in the main fields of their application—the synthesis of polymers and dyes—tetracarboxylic acids enter into a reaction with amines and the products of this reaction are subjected to intramolecular dehydration with formation of cyclic structures. Here it is noteworthy that the size of the ring formed corresponds to the size of the anhydride of the initial acid. Subsequently the term "tetracarboxylic acid" will be applied only to acids capable of forming five-, six-, and seven-membered internal cyclic dianhydrides.

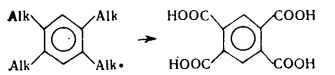
Among the numerous method of synthesising carboxylic acids [6], the following have found application in the preparation of the compounds in which we are interested: oxidation of organic compounds, cycloaddition reactions, condensation of dicarboxylic acids and their derivatives, and malonic ester syntheses. In addition there are several non-general methods, specific to the given tetracarboxylic acid.

II. OXIDATION OF ORGANIC COMPOUNDS

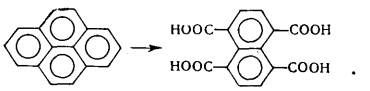
Hitherto the oxidation of organic compounds has been essentially the only method of synthesising tetracarboxylic acids having extensive practical applications. This is because oxidation reactions are particularly suitable for the synthesis of aromatic tetracarboxylic acids on the basis of which polymers with the most valuable properties have been obtained. The method of oxidation has already been applied on an industrial scale, although the range of products manufactured is fairly narrow.

The method can be clearly divided into three types in terms of the compound undergoing oxidation.

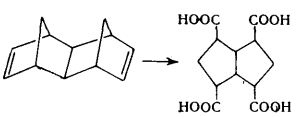
A. Oxidation of side chains in aromatic hydrocarbons, for example:



B. Oxidation of the rings of polynuclear aromatic compounds, for example:



C. Oxidative cleavage of olefins, for example:



The same reagents are used in laboratory practice for all three types of reactions: nitric acid, permanganates, chromates, dichromates, ozone, peroxides, and hypochlorites. Therefore initially we shall briefly characterise the scope and mechanism of the action of each of these substances.

The oxidation of hydrocarbons to acids is a multistage process and proceeds as a rule according to the following scheme: hydrocarbon → alcohol → aldehyde (ketone) → carboxylic acid. The slowest stage is the oxidation of the C–H or C–C bonds, while the subsequent stages take place with increasing ease: the alcohol is oxidised more readily than the hydrocarbon and the aldehyde more readily than the alcohol[7].

All organic compounds can be oxidised by hot nitric acid which need not necessarily be very concentrated for this purpose. This reagent is particularly active in the vapour phase[6]. The oxidation proceeds via a homolytic mechanism and includes stages involving the formation and decomposition of nitro-compounds, nitrates, and nitrites[7]. Chain reactions take place at some of the stages and nitro-compounds and nitrates do not accumulate in the course of the reaction. However, the contamination of the final product by nitrogen-containing compounds is one of the principal disadvantages of oxidation with nitric acid.

Chromic acid, chromates, dichromates, and chromyl chloride are more selective than nitric acid. They are capable of oxidising only activated C–H bonds in allyl and benzyl groups, at tertiary carbon atoms, and carbon atoms adjoining a heteroatom[7]. The reaction is usually carried out in dilute sulphuric acid solutions but aqueous solutions of alkali and glacial acetic acid can be employed.

The oxidation by chromates of the side chains in aromatic hydrocarbons and of alcohols and aldehydes constitutes a heterolytic process including a stage in which a new C–O–Cr linkage is formed. In the oxidation of alcohols by chromic acid, the first stage is rapid and reversible esterification and the rate of the overall process is limited by that of the stage of the concerted decomposition of the ester[8].

The oxidation of olefins involves a direct electrophilic attack on the π electrons of the C–C bond by one of the oxygen atoms of the reagent. The reaction is more difficult than with alcohols, so that the oxidation takes place only in acid media. Chromates attack aromatic compounds at the carbon atom with the highest electron density, for example they oxidise anthracene to anthraquinone[9].

Permanganates are very powerful reagents capable of oxidising in neutral, alkaline, and acid aqueous media and also in organic solvents—acetone or pyridine. In contrast to chromates, the oxidation of benzyl C–H bonds by permanganate involves a hydride transfer stage[7], for example:

$$MnO_4^- + H-\overset{|}{\underset{|}{C}}-O^- \rightarrow \overset{|}{\underset{|}{C}}=O + (HMnO_4)^{3-}$$

This reaction is catalysed by both acids and bases, but alkaline solutions are not used for extensive oxidation, since the process is complicated by the Cannizzaro reaction in the aldehyde formation stage.

When acted upon by permanganates in a neutral or acid medium, olefins initially give rise to acyloins, which are then rapidly oxidised until the attainment of more advanced stages[7,8]. A disadvantage of this reagent is the necessity to separate the reaction products from the manganese dioxide precipitate.

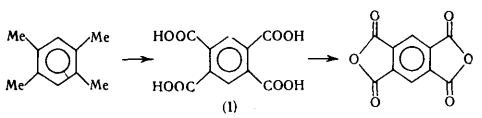
Ozone is used to oxidise condensed polynuclear hydrocarbons and for the oxidative cleavage of olefins. In the synthesis of acids, ozonides are decomposed by peroxides, peracids, oxygen, activated ozone, metal salts, etc.[10] In contrast to NO_2^+ or chromates, which attack the most nucleophilic carbon atom of the polynuclear compound, ozone is a test reagent for the most reactive double bond[11]. Thus pyrene is oxidised by ozone to biphenyl-2,2',6,6'-tetracarboxylic acid, while nitric acid and permanganate oxidise it to naphthalene-1,4,5,8-tetracarboxylic acid[12].

Hypochlorites and peroxides are effective reagents for the oxidation of polynuclear quinones to carboxylic acids. Initially one usually oxidises aromatic hydrocarbon by nitric acid, chromate, and permanganate to quinones and the latter are then treated with hypochlorite or hydrogen peroxide, which leads to acids in almost quantitative yields[13].

All the oxidation reactions enumerated above make it possible to obtain acids in yields reaching 90–95% and the oxidation methods have been fairly thoroughly developed and to some extent standardised.

1. Oxidation of Side Chains of Aromatic Hydrocarbons

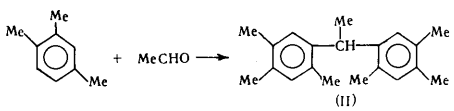
Since 1851 when Erdmann[14] obtained for the first time benzene-1,2,4,5-tetracarboxylic (pyromellitic) acid (I) (PMA) and its anhydride by oxidising durene with nitric acid, PMA has been for about 100 years virtually the only readily available aromatic tetracarboxylic acid obtained by this procedure. However, this method of synthesising tetracarboxylic acids (primarily PMA) has acquired practical importance only recently as a result of the development and improvement of the oxidation technology and methods of synthesising and purifying the initial alkylbenzenes:



(I)

The principal difficulty in the synthesis of PMA is that the initial 1,2,4,5-tetramethylbenzene (durene) is very difficult to free from isomers. In this connection three procedures have been outlined for the preparation of pure PMA: by developing methods of synthesising pure durene, by obtaining PMA from sources other than durene, and by devising methods for the separation of PMA from isomeric acids and for its purification.

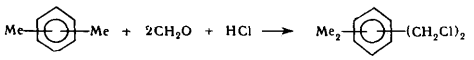
Pure durene is obtained by the hydrocracking of 1,1-dipseudocumenylethane (II), which is obtained by treating pseudocumene with acetaldehyde (yield 96%, purity 99.1%):[15-17]



(II)

The direct oxidation of (II) or durene obtained by the hydrocracking of (II) leads to pure PMA.

The greatest success was achieved by the second procedure in the chloromethylation of crude xylene[18]:



(III)

Di(chloromethyl)xylene isomers are readily separated by simple crystallisation. The pure 1,2,4,5-isomer is chlorinated further to the tetrachloro-derivative and then oxidised. This method was modified somewhat recently[19,20]: 4,5-di(hydroxymethyl)-1,2-dimethylbenzene, obtained by treating (III) with alkali, is oxidised. In both cases the reaction product is very pure PMA.

There are also methods of synthesising PMA from $1,2,4,5\text{-}R_n\text{-}(HOOC)_{4-n}C_6H_2$, where R is a small alkyl

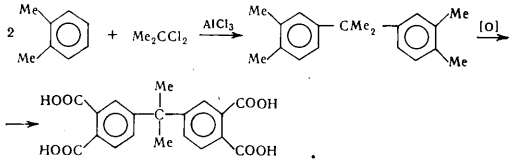
group and $n = 1-4$,[21] 2,5-di-isopropyl-1,4-dimethylbenzene obtained by propylating *p*-xylene or pseudocumene in the presence of Al_2O_3 and BF_3,[22] and also many other alkylbenzenes[17]. So far these methods have not acquired practical importance.

The possibility of isolating PMA from a mixture of isomeric acids is due to the fact that benzene-1,2,3,4-tetracarboxylic (mellophanic) acid isomerises to PMA at 330–340°C. For example, by refluxing a mixture of PMA and mellophanic acid in trichlorobenzene, one obtains fairly pure PMA.[23]

There are also methods whereby PMA obtained by oxidation with nitric acid can be freed from nitrogen-containing impurities by partition chromatography at 100 to 110°C (purity 98%),[24] by passing heated air or an inert gas through the acid melt at 300°C (purity 98.6%),[23] and by treatment with reducing agents—acetaldehyde, formaldehyde, and hydroquinone—at 200–210°C and a pressure of 45–70 atm.[25] The PMA dianhydride is purified by recrystallisation from a dioxan–acetic anhydride mixture[26] and via complexes with dimethylformamide (DMF)[27] or chlorine-containing aromatic compounds[28].

Apart from PMA, a number of other aromatic tetracarboxylic acids obtained by the oxidation of side chains have been known since the beginning of this century. These compounds were synthesised by the usual method for the oxidation or demonstration of the structures of alkyl derivatives of aromatic compounds or were obtained as intermediates. Thus mellophanic acid was obtained by oxidising the corresponding tetramethyl- and tetraethylbenzenes with permanganate[29]; biphenyl-3,3′,4,4′-tetracarboxylic acid was synthesised by oxidising 3,3′-dimethylbiphenyl-4,4′-dicarboxylic acid[30]; the oxidation of 2,3,6,7-tetramethylanthraquinone yielded anthraquinone-2,3,6,7-tetracarboxylic acid and its reduction gave anthracene-2,3,6,7-tetracarboxylic acid; pyridine-2,3,5,6-tetracarboxylic acid was obtained from 3,5-dicarboxy-2,6-dimethylpyridine[32]; benzoquinonetetracarboxylic acid was synthesised from durene via dinitropyromellitic and diaminopyromellitic acids[33]. The oxidation method has been used for the specific synthesis of products of practical value only since the appearance of new applications of tetracarboxylic acids.

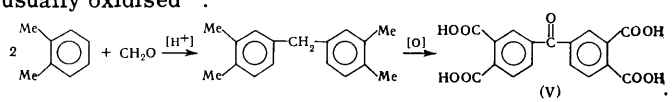
A method for the oxidation of 2,2,-di-(*o*-xylyl)propane, obtained by the Friedel–Crafts reaction between *o*-xylene and 2,2-dichloropropane, to 2,2,-di-(3,4-dicarboxyphenyl)-propane (IV) was patented as early as 1955:[34]



(IV)

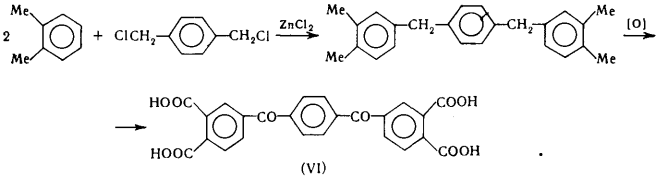
This procedure was subsequently extended to other alkylenediphthalic acids[35].

Several methods of synthesising the initial alkyl derivatives were developed in order to obtain benzophenone-3,3′,4,4′-tetracarboxylic acid (V). Di-(*o*-xylyl)methane is usually oxidised[36]:



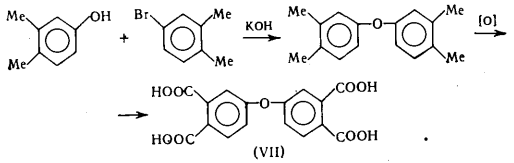
(V)

Di-(*o*-xylyl)ethane and other 1,1-di-(*o*-xylyl)alkanes[37], di-(*o*-xylyl)ethylene[38], and di-(*o*-xylyl) ketone obtained by the Friedel–Crafts reaction between *o*-xylene and phosgene[39], have also been used. The last method has been employed to synthesise a tetracarboxylic acid with two keto-groups (VI):[40]



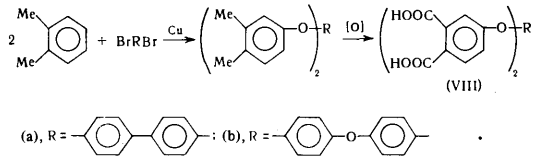
(VI)

By oxidising the products of the reaction of 3,4-dimethylphenol with 4-bromo-*o*-xylene in the presence of alkali, di-(3,4-dicarboxyphenyl) ether (VII) was obtained[35]:



(VII)

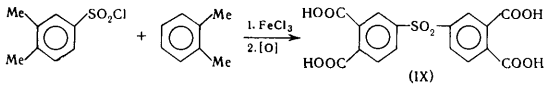
The acids (VIIIa) and (VIIIb) were obtained in low yields by a similar procedure[41]:



(VIII)

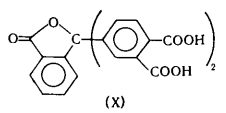
(a), R = ; (b), R =

Di-(3,4-dicarboxyphenyl) sulphone (IX) is formed by oxidising the corresponding tetramethyl derivative[42], which is obtained either by the reaction of thionyl chloride with *o*-xylene in the presence of aluminium chloride[43] or by the reaction of *o*-xylenesulphonyl chloride with *o*-xylene[44]:



(IX)

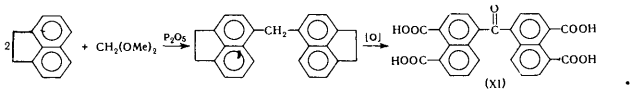
Korshak and coworkers[45] developed a procedure for the synthesis of the tetracarboxylic acid (X) by oxidising 3,3-di(3,4-dimethylphenyl)phthalide with permanganate in pyridine and then in water:



(X)

Yet another version of the side chain oxidation method involves the use of acenaphthene derivatives as starting materials. Thus the oxidation of 3,4-dicarboxyacenaphthene by nitrogen oxides and treatment of the resulting intermediate acenaphthenequinone with hypochlorite or hydrogen peroxide yielded naphthalene-1,2,4,5-tetracarboxylic acid[46,47].

The synthesis of the very interesting dianhydride of the tetracarboxylic acid (XI), involving the oxidation of bisacenaphthenyl derivatives, has been developed[48]:



(XI)

Compound (XI) is also obtained by the oxidation of diacenaphthenyl ketone synthesised by the Friedel–Crafts reaction between acenaphthene and phosgene. The

method of oxidising side chains is also suitable for the preparation of acids containing organic groups combined with various elements. The oxidation of phenyldi-(3,4-xylyl)-phosphine yielded di-(3,4-dicarboxyphenyl)phenylphosphine oxide used in the synthesis of polyimides[49], and treatment of dixylylcarboranes with CrO_3 leads to the corresponding tetracarboxylic acid in a yield of about 50% in the oxidation stage[50].

The method has been used industrially to synthesise pyromellitic dianhydride by the liquid-phase (with nitric acid) and vapour-phase oxidation of the side chains of tetra-alkylbenzenes. It is noteworthy that the principal characteristics of the oxidation of durene and other tetra-alkyl derivatives of aromatic hydrocarbons are analogous to those of the thoroughly investigated mechanism of the oxidation of *o*-xylene to phthalic anhydride[51].

The oxidation of durene with nitric acid leads to PMA in high yields, but the product contains a large amount of impurities which are difficult to separate, mainly nitro-compounds[52]. The use of nitric acid requires the application of expensive corrosion-resistant apparatus, which, together with the cost of pure durene makes this process relatively uneconomical. At present the liquid-phase oxidation of durene is hardly used to synthesis PMA. However, nitric acid is employed to oxidise chloromethylated xylenes to PMA intended for the synthesis of polyimides. In this case there is a possibility of obtaining high-purity PMA without the need for additional operations[20,53].

The industrial methods for the preparation of PMA dianhydride on the largest scale involves the catalytic vapour-phase oxidation of durene and other tetra-alkylbenzenes by atmospheric oxygen[54-57]. Vanadium pentoxide is the active component of the catalyst. The process is carried out by a continuous process and the yield of products in one cycle is 60% (90%) with respect to the alkylbenzene consumed[58,59]. There is also a method involving the almost complete oxidation of durene to PMA dianhydride in one cycle with 98% purity (the principal impurity is PMA).[60]

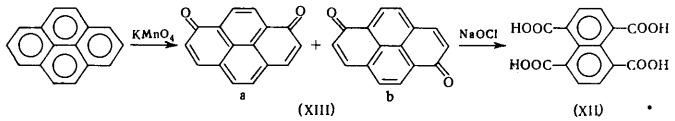
The main advantage of the vapour-phase oxidation method is the simplicity of the apparatus required for this process. The reaction is carried out in apparatus and with catalysts employed for the vapour-phase oxidation of *o*-xylene, which permits cheap large-scale manufacture of PMA. The cost of PMA obtained by the vapour-phase oxidation is lower by a factor of 3–5 than that of the product synthesised by oxidation with nitric acid[60].

The examples quoted illustrate fairly completely the scope of the method of oxidation of side chains of aromatic compounds, which is at present the principal method for the synthesis of aromatic tetracarboxylic acids. In all cases the yield of acids in the oxidation stage approaches 90%. However, we have consistently drawn attention to the synthesis of substances undergoing oxidation. The simpler and more reliable the oxidation stage the more complex are the methods of synthesising and purifying the initial alkyl derivatives. As a rule, the yield of acids barely exceeds 50% when account is taken of the synthesis of the initial compound, and the key starting materials—pure *o*-xylene and particularly durene—are at present fairly expensive.

2. Oxidation of the Rings of Polynuclear Aromatic Compounds

A typical example of the oxidation of condensed aromatic compounds is the treatment of graphite with hot nitric acid, which leads to a mixture of mono- and polycarboxybenzenes. The oxidation of graphitised charcoal has been suggested for the synthesis of aromatic acids[61,62]. However, this method lacks practical importance owing to the complexity of the isolation of the individual compounds, although there is a procedure for the separation of acids by fractionating the esterification products[63].

The most important reaction of this method is the oxidation of pyrene to naphthalene-1,4,5,8-tetracarboxylic acid (XII). When pyrene is oxidised by permanganate or dichromates, 1,8- and 1,6-pyrenequinones (XIIIa) and (XIIIb) are formed initially and are then oxidised by hypochlorite in an alkaline medium to (XII):[64-66]

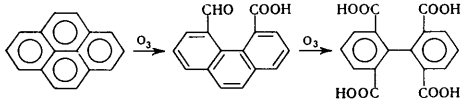


(XIII) (XII)

The method of synthesising (XII) from 1,3,6,8-tetrachloropyrene formed in high yields by the chlorination of pyrene in tetrachloroethane, is convenient. Treatment of the chloro-derivative with concentrated nitric acid or oleum leads to di-*peri*-naphthindandione, which is oxidised by nitric acid, manganese dioxide in sulphuric acid, or hypochlorite to (XII).[67,68]

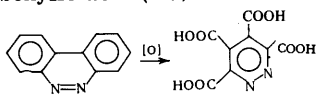
Derivatives of (XII) containing SO_3H, OH, OR, NO_2, and NH_2 groups in the ring, formed on oxidising substituted 5,6-dicarboxyacenaphthenes, are also available[69].

On ozonolysis, pyrene absorbs two moles of ozone, biphenyl-2,2',6,6'-tetracarboxylic acid (XIV) being formed in 60% yield after the decomposition of the ozonides[12,70]:



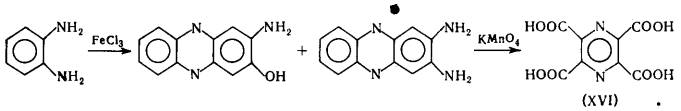
(XIV)

The ring oxidation method is very useful for the synthesis of heteroaromatic acids, since rings free from electronegative heteroatoms are more readily oxidised in polynuclear compounds. Thus the oxidation of phenazone by an alkaline solution of permanganate leads to pyridazinetetracarboxylic acid (XV):[71]



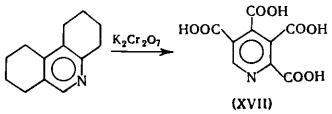
(XV)

Pyrazinetetracarboxylic acid (XVI) is formed via the mechanism[72]:



(XVI)

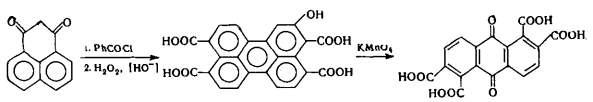
The oxidation of phenanthridine, obtained by treating cyclohexanone with formaldehyde, ammonium acetate, and ammonium hydroxide, resulted in the synthesis of pyridine-2,3,4,5-tetracarboxylic acid (XVII):[73]



(XVII)

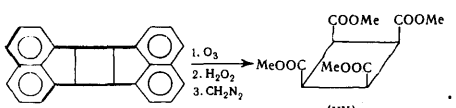
In order to illustrate the scope of this method, one may mention the synthesis of biphenyl-2,3,5,6-tetracarboxylic acid by oxidising 1-phenylnaphthalene-2,3-dicarboxylic

acid [74] and the synthesis of hydroxyperylenetetracarboxylic acid (XVIII) and anthraquinone-1,2,5,6-tetracarboxylic acid (XIX): [75]



(XVIII) (XIX)

The synthesis of an aliphatic tetracarboxylic acid by the ozonolysis of β-heptacyclene—an acenaphthene dimer—constitutes an interesting example. The decomposition of the ozonide with hydrogen peroxide and treatment with diazomethane lead to the ester (XX): [76]

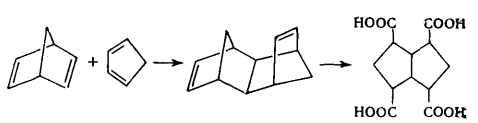


(XX)

The method of oxidation of polynuclear aromatic compounds has all the advantages and disadvantages of the side chain oxidation method discussed above. The method is of greatest value for the synthesis of naphthalene-1,4,5,8-tetracarboxylic acid—one of the cheapest and most readily available tetracarboxylic acids.

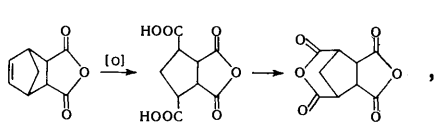
3. Oxidative Cleavage of Olefins

A classical example of the synthesis of tetracarboxylic acids by oxidative cleavage of olefins is provided by the synthesis of bicyclo[3,3,0]octane-2,4,6,8-tetracarboxylic acid (XXI) from hexahydro-1,4,5,8-*exo*,*endo*-dimethanonaphthalene [77,78]:

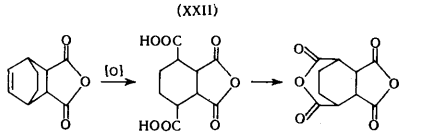


(XXI)

Diels–Alder adducts of maleic anhydride and cyclic dienes, for example cyclohexa-1,3-diene and cyclopenta-1,3-diene, are used as the compounds oxidised in other cases. After oxidation, a mixture of the stereoisomeric tetracarboxylic acid (XXII) and (XXIII) is formed [79]:



(XXII)



(XXIII)

The oxidation is carried out with nitric acid and permanganate, but best results have been obtained by the ozonolysis of the adducts followed by treatment with peracetic acid [80].

It is noteworthy that *endo*-methylenetetrahydrophthalic acids have recently become readily available, since a method has been devised for their synthesis by treating with maleic anhydride the C_5-fraction from the cracking of light petroleum.

The range of tetracarboxylic acids which can be readily obtained by the oxidative cleavage of double bonds is limited to the products enumerated above. Although the preparative aspect of the method is simple and the overall yield of products is close to 90%, their structures preclude their employment in the applications of tetracarboxylic acids known at present.

III. CYCLOADDITION REACTIONS

Cycloaddition reactions are understood as electrocyclisation processes involving polyenes in which new σ bonds are formed as a result of the opening of the π bonds in the groups added. Such reactions include processes involving the formation of at least two σ bonds, i.e. $2\pi \rightarrow 2\sigma$, $3\pi \rightarrow 3\sigma$, and $4\pi \rightarrow 4\sigma$ reactions. Only the most common $2\pi \rightarrow 2\sigma$ reactions have found application in the synthesis of tetracarboxylic acids. Such processes are observed in 2 + 2, 4 + 2 (the Diels–Alder reaction), 4 + 4, and 6 + 4 cycloadditions.

According to Woodward–Hoffmann rules [82-84], the mode of the concerted single-stage electrocyclisation reactions and also the stereochemistry of the adducts formed are determined by the symmetry of the π orbitals involved and formed in the reaction. This type of cycloaddition is possible only when the molecular orbitals involved in the reaction are correlated, without an energy barrier, with the molecular orbitals of the reaction product. For thermal reactions proceeding via the molecular ground state, the symmetry of the highest occupied π orbital is of decisive importance and in photochemical reactions involving excited states the mode of reaction depends on the symmetry of the lowest unfilled orbital. Since the symmetries of these orbitals are different, it follows that, when a given type of cycloaddition is allowed in the thermal reaction, it is forbidden in photochemical electrocyclisation processes.

According to the selection rules, $2\pi \rightarrow 3\sigma$ processes are thermally allowed for systems in which the number of π electrons involved in the reaction is $4n + 2$ and photochemical reactions are allowed for systems in which the number of π electrons is $4n$.

This conclusion is of fundamental importance for cycloaddition reactions, since it determines both the structure of the product formed and its stability. One may conclude that photo-adducts are thermally stable, since, in accordance with the principle of microscopic reversibility, their thermal dissociation is a forbidden process.

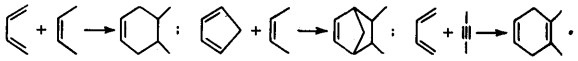
The characteristics of electrocyclisation reactions discovered by Woodward and Hoffmann constitute, in particular, a theoretical justification of Alder's empirical rules [85] for 4 + 2 cycloadditions and are confirmed by very extensive experimental data.

The two most common types of cycloadditions—thermal 4 + 2 and photochemical 2 + 2 processes—as well as their combinations have found the widest applications in the synthesis of tetracarboxylic acids and their functional derivatives.

1. The Diels–Alder Reactions (4 + 2 Cycloaddition Reactions)

The Diels–Alder reaction or diene synthesis involves the addition of olefins or acetylenes (dienophiles) to the

1,4-positions of *cis*-1,3-dienes with formation of unsaturated six-membered cyclic compounds (adducts):



Electron-donating substituents in the diene and particularly electron-accepting substituents in the dienophile facilitate the addition and the latter factor is responsible for the extensive scope of this method in the synthesis of carboxylic acids. Indeed the carboxy-group and its functional derivatives exhibit a powerful electron-accepting effect and $\alpha\beta$-unsaturated acids are active dienophiles. The interaction of compounds containing two diene systems, or compounds capable of their formation, with $\alpha\beta$-unsaturated $\alpha\beta$-dicarboxy-derivatives constitutes a direct method for the synthesis of tetracarboxylic acids and the use of maleic anhydride—one of the most powerful dienophiles—leads directly to the anhydrides.

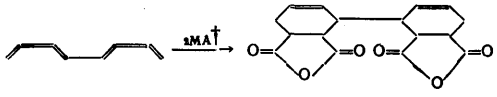
The Diels–Alder reaction can be carried out on a preparative scale without difficulty—by simple mixing of the components, frequently in an inert solvent—and heating to moderate temperatures leads to adducts, as a rule in high yields.

There is no need to discuss the principal characteristics and mechanism of the diene synthesis, since these problems have been considered in many monographs [85–87] and reviews [88,89]. We shall mention only one very important factor: the Diels–Alder reaction is a reversible process and elevated temperatures favour the dissociation of the adducts into the initial components (the retrodiene synthesis).

However, there are several procedures whereby one can synthesise adducts incapable of the retrodiene synthesis or requiring for dissociation temperatures at which single carbon–carbon bonds are ruptured.

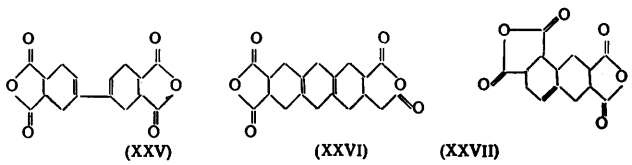
The first of these is based on the fact that the greater the energy gain on conversion of the initial compounds into the adducts the higher the temperature at which the adduct undergoes the retrodiene synthesis. Hence follows the practically important conclusion that open-chain bisdiene adducts should decompose at fairly high temperatures. Indeed acyclic bisdienes are involved in cycloaddition in a thermodynamically unstable conformation with pairs of cisoid double bonds, and their adducts are substituted cyclohexene structures with minimal Baeyer strain.

This conclusion has been confirmed experimentally. Octa-1,3,5,7-tetraene forms with maleic anhydride an adduct (XXIV) in almost quantitative yield, having a decomposition temperature in excess of 280°C: [90]



(XXIV)

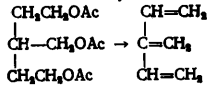
The dianhydrides (XXV)–(XXVII) also melt without decomposition at temperatures comparable to the melting points of their aromatic analogues [91–93]:



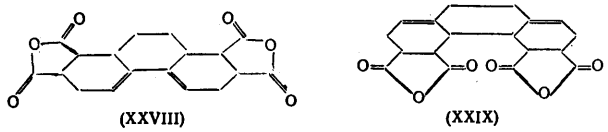
(XXV) (XXVI) (XXVII)

† In the formulae MA denotes maleic anhydride.

The starting compounds for the synthesis of these bisadducts are tri- and tetra-enes obtained by a general method—the pyrolysis of acetyl derivatives of tri- and tetra-hydric alcohols at 550°, for example:



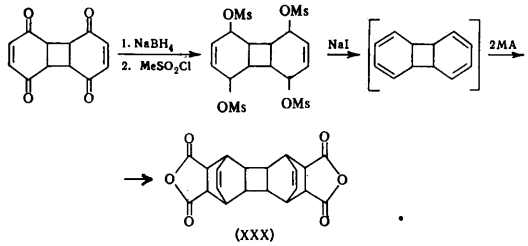
Thermal isomerisation of cyclodeca-1,2,6,7-tetraene yielded 2,3-divinylcyclohexa-1,3-diene, which combined with two molecules of maleic anhydride to form the dianhydride (XXVIII). [94] In the presence of an excess of the dienophile, compound (XXVIII) forms a trianhydride:



(XXVIII) (XXIX)

Similarly 1,4-divinylcyclohexa-1,3-diene (obtained from 1,4-diethynylcyclohexane-1,4-diol) yields the dianhydride (XXIX). [95]

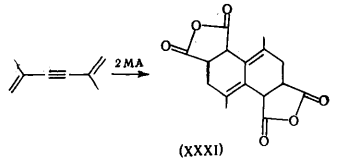
Sometimes the difference between the thermodynamic stabilities of the diene and the adduct is so great that even with cyclic bisdienes the equilibrium in the diene synthesis reaction is completely displaced to the right. Thus the tetramethylsulphonate of the reduced photo-dimer of *p*-benzoquinone yields the dianhydride (XXX) on treatment with sodium iodide in the presence of maleic anhydride, but the corresponding bisdiene cannot be isolated [96]:



(XXX)

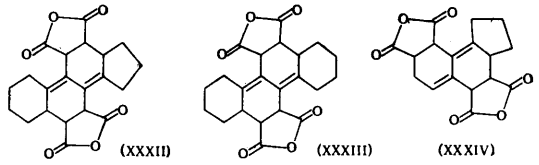
Compound (XIX) does not melt up to 360°C and sublimes without decomposition at 250°.

There is a method of synthesising dianhydrides involving the addition of two molecules of the dienophile to substituted 1,5-dien-3-ynes [97]. For example, 2,5-dimethylhexa-1,5-dien-3-yne yields the dianhydride of hexahydronaphthalenetetracarboxylic acid (XXXI): [98]



(XXXI)

Dienynes in which one or both double bonds are in cyclic systems are also reactive in this reaction. Thus cyclohex-1-en-ylcyclopent-1-enylacetylene, di(cyclohex-1-enyl)acetylene, and cyclopent-1-enylisopropenylacetylene form with two molecules of maleic anhydride the bisadducts (XXXII)–(XXXIV) [99–101] having decomposition temperatures in excess of 260°C:

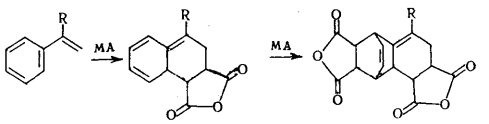


(XXXII) (XXXIII) (XXXIV)

The addition of dienophiles to 1,5-diene-3-ynes differs from the reactions of bisdienes enumerated above by the fact that in this case the adduct is formed with simultaneous addition of two dienophile molecules to the diene, i.e. via a trimolecular reaction.

In assessing the method of synthesis of dianhydrides involving open-chain bisdienes, one should note that it suffers from a fundamental deficiency—the difficulty of obtaining the starting compounds. The achievement of a high thermal stability of the bisadducts requires in this instance thermodynamically unstable bisdienes, i.e. the very principle of the method is responsible for the difficulty of synthesising the initial compounds on a preparative scale. As a rule, acyclic bisdienes are obtained by multistage procedures with very low yields of the final products. For example, in the pyrolysis of acetates, the yield of bisdienes does not exceed 5–15% and dienynes are obtained in a yield of 10–30%.

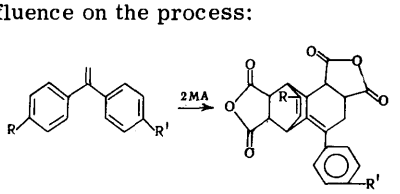
The method of synthesising the dianhydrides by the Wagner–Jauregg reaction [102], in which substituted styrenes or 1,1-diarylethylenes are employed as the bisdienes, is free from this disadvantage. In the first stage, a molecule of maleic anhydride is added to a system including an exocyclic double bond and the π electrons of the α- and β-carbon atoms of the aromatic ring with formation of the adduct (XXXV). The addition of a second molecule of the dienophile to the newly formed diene system leads to the dianhydride (XXXVI): [103]



(XXXV) (XXXVI)

Although, owing to its tendency towards polymerisation, styrene itself gives low yields of adducts by this reaction [104], its α-substituted analogues form adducts in yields of 90%, particularly in the presence of polymerisation inhibitors. Many dianhydrides having the general formula (XXXVI) with R = alkyl, halogen, phenyl, naphthyl, etc., melting at 220–300°C, have been synthesised by this method [103,105,106]. β-substituted styrenes do not form bisadducts as a rule [106].

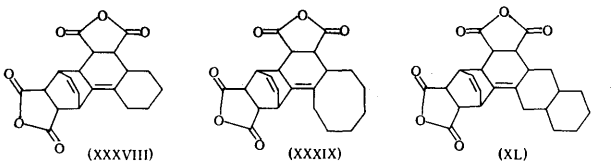
The efficiency of cycloaddition is appreciably influenced by the electronic nature of the substituents in the *para*-position of the aromatic ring. It has been shown [107] that electron-donating substituents, particularly the methoxy-group, facilitate the reaction, while electron-accepting substituents frequently make the reaction impossible, as has been observed also in other Diels–Alder reactions. Substituents in the *meta*-position hardly affect the course of the reaction, and *ortho*-derivatives are usually inactive owing to the steric hindrance to the planarity of the system. Substituents in the aromatic ring of 1,1-diarylethylenes not involved in the diene synthesis have a similar influence on the process:



(XXXVII)

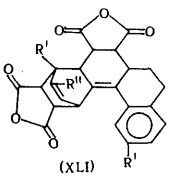
Thus the yield of the dianhydrides (XXXVII) varies from 22% for the difluoro-derivatives to 90% for the di-t-butyl analogue, while the melting point varies in the opposite sense: from 350° to 240°C respectively.

Arylcyclenes—compounds with a double bond in a partly hydrogenated ring—are also reactive in the Wagner-Jauregg reaction [108,109]. For example cyclohex-1-enylbenzene, cyclo-oct-1-enylbenzene, and 2-phenyl-Δ^2-octahydronaphthalene form the adducts (XXXVIII)–(XL) respectively in high yields:



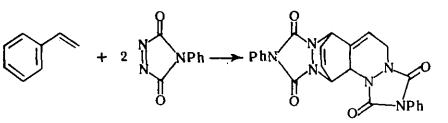
(XXXVIII) (XXXIX) (XL)

A number of substituted dianhydrides (XLI) based on 1-phenyl-3,4-dihydronaphthalene, where R, R′, and R″ are combinations of H, CH_3, C_6H_5, Cl, and OCH_3 groups, with melting points up to 300°C, have also been synthesised [108].



(XLI)

The use of a more powerful dienophile—4-phenyl-1,2,4-triazoline-3,5-dione—made it possible to obtain the bisadduct (XLII) by the reaction with styrene [110]:



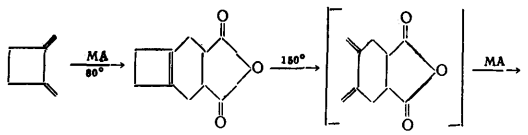
(XLII)

Since all the dianhydrides obtained by the Wagner-Jauregg reaction have a sterically strained tricyclic structure, they split off smoothly one dienophile molecule above the melting point. However, the melting points of the bisadducts reach 350°C and the decomposition temperatures are comparable to the temperatures at which carbon–carbon single bonds are ruptured, which, together with the ready availability of the initial compounds and the high yield of the desired products, suggests that the method is of practical value.

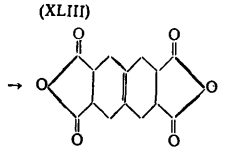
All the procedures for the application of the 1,4-addition reaction in the synthesis of tetracarboxylic acids enumerated above involve a reversible adduct formation stage. On the other hand, there is a fundamentally different type of Diels–Alder reaction in which, simultaneously with the addition of the dienophile to the diene, the adduct undergoes irreversible changes, in relation to the initial diene, associated with the rupture of chemical bonds.

For example, 1,2-dimethylcyclobutane, obtained by the dimerisation of allene, gives the adduct (XLIII) in 94% yield on refluxing with maleic anhydride in benzene. When the temperature is raised to 150°C, a bond in the cyclobutane ring of (XLIII) is cleaved with formation of a diene

system the addition of a dienophile to which gives rise to the dianhydride (XLIV):[111]

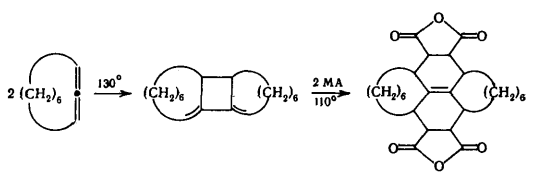


(XLIII)



(XLIV)

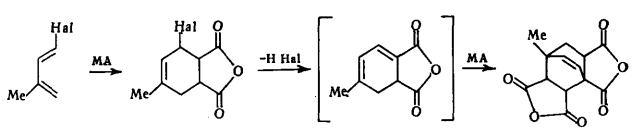
A similar procedure has been used[94] to synthesise the dianhydride (XLV), which melts without decomposition above 300°C:



(XLV)

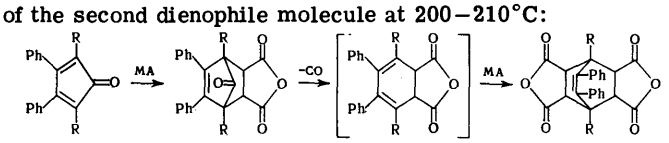
However, irreversible Diels–Alder reactions are usually accompanied by the abstraction of volatile substances from the intermediate.

A method has been suggested[112] for the synthesis of the adduct (XLVI) using 1-halogeno-3-methylbuta-1,3-dienes (obtained from ethynyldimethylmethanol) as the bisdienes. Compound (XLVI) is obtained in an exothermic reaction with liberation of the hydrogen halide:



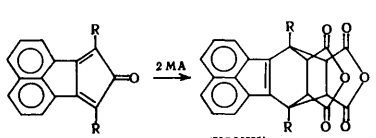
(XLVI)

Reactions are also known in which carbon monoxide is split off from the intermediate adduct. These reactions involve the use of cyclopentadienones (cyclones) as the dienes. 3,4-Diphenylcyclones, formed on dehydration of anhydroacetone benzils, are the most suitable for this purpose. The bisadducts (XLVII, R and R′ = H or alkyl) are formed in quantiative yields[113–116]. The decarbonylation is as a rule carried out with the simultaneous addition of the second dienophile molecule at 200–210°C:



(XLVII)

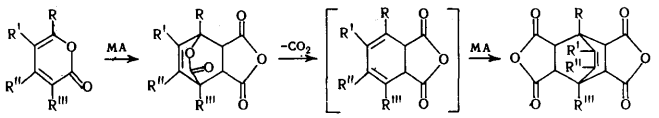
Condensed cyclones react similarly; for example an acecyclone yields the dianhydride (XLVIII, R = methyl or n-hexyl)[117]:



(XLVIII)

Dianhydrides of a similar type are also formed when α-pyrones or coumalins, the adducts of which split off a carbon dioxide molecule, are employed as the bisdienes[118].

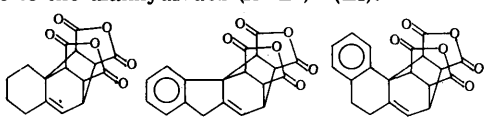
The reaction proceeds via the mechanism



(XLVII)

The synthesis of a whole series of alkyl- and phenyl-substituted derivatives (XLVII) has been described by Shusherina and coworkers[119,120]. The preparation of the perchloro-1,4-diphenyl derivative of (XLVII) and also the continuous method for the synthesis of the dianhydride of bicyclo[2,2,2]oct-7-ene-2,3,5,6-tetracarboxylic acid (XLVII, all R = H) in 99% yield have been patented[121–123].

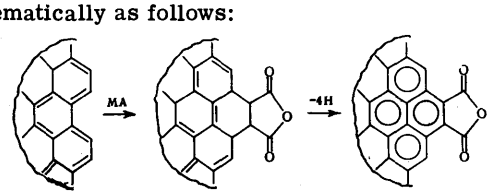
Dianhydrides with decomposition temperatures in excess of 300°C, obtained on the basis of condensed coumalins, are also known. Thus 5,6-dicyclohexano- and 5,6-indeno-α-pyrones and 7,8-benzo-5,6-dihydrocoumarin give rise to the dianhydrides (XLIX)–(LI):[124]



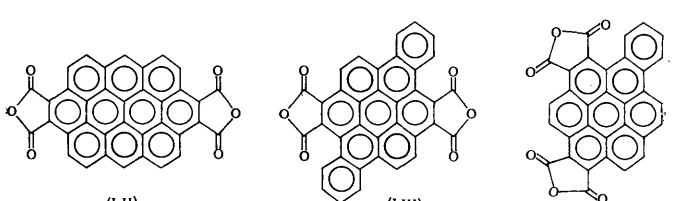
(XLIX) (L) (LI)

Adducts of type (XLVII) decompose above the melting point with liberation of maleic anhydride, i.e. reactions of this type are not strictly speaking irreversible. However, the dissociation reaction occurs at 320–350°C and is accompanied by the decomposition of the product by other mechanisms too.

Clar[125] developed a method for the synthesis of dianhydrides involving the addition of maleic anhydride to polycyclic aromatic structures with simultaneous dehydration of the adducts formed. The method can be represented schematically as follows:



The dehydrogenation is carried out either with chloranil added to the melt of the components or by refluxing the substances to be added in an active solvent—nitrobenzene. Dianhydrides based on bisanthene, 2,3:8,9-dibenzoperylene, 1,2:4,5-dibenzopyrene, 1,2:4,5:8,9-tribenzopyrene, and di-*peri*-naphthyleneanthracene have been obtained by this method—for example the dianhydrides (LII)–(LIV):[126–129]



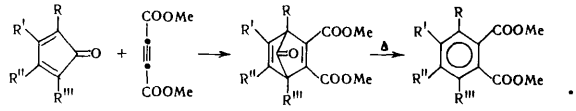
(LII) (LIII) (LIV)

This method is so far of purely theoretical importance, since the initial bisdienes are very difficult to obtain and most of them are very active carcinogens.

All the methods of preparation of tetracarboxylic acids by the Diels–Alder reaction known hitherto lead to products with hydroaromatic or bicyclic structures. On the

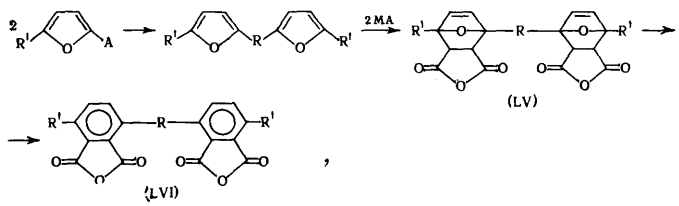
other hand, aromatic acids are necessary for the main applications of tetracarboxylic acids—the synthesis of thermostable polymers and dyes.

Certain types of monoadducts obtained in the 1,4-cycloaddition reaction propagated by thermal or chemical factors are known [85] to undergo a rearrangement into aromatic structures. For example, the adducts of dimethyl acetylenedicarboxylate and cyclones split off a carbon monoxide molecule on heating and form phthalic acid esters:

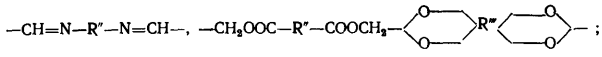


Adducts of coumalins with acetylenes, of furans with maleic anhydride, and certain others are also capable of aromatisation.

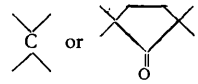
The authors of the present review [130-136] developed a method for the synthesis of tetracarboxylic acids the main idea of which involves the aromatisation of the adducts of maleic anhydride with bisfuran compounds via the general mechanism



where A is a functional group or a hydrogen atom, R = arylene,



R′ = aryl (for example phenyl) or a hydrogen atom,
R″ = arylene (*p*-phenylene, *pp*′-diphenylene, and others),

and R‴ =  .

The use of bisfuran compounds in these reactions has many advantages. Firstly, the furan ring is a fairly reactive diene in reactions with maleic anhydride and forms stable adducts in yields of 90–95%. Secondly, the synthesis of compounds containing two furan rings can be readily achieved with a high yield when readily available and cheap functional derivatives of furan are employed: furfural, furfuryl alcohol, furancarboxylic acids, etc.

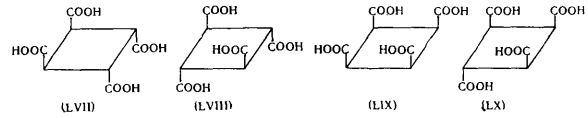
Bisfuran compounds have been obtained by the decomposition of diazonium salts in furan, by the reaction of furfural with aromatic amines or tetramethoxy-derivatives, for example pentaerythritol, and by the reaction of furfuryl alcohol with aromatic dicarboxylic acid esters.

The reactions of bisfuran with maleic anhydride occur at a temperature as low as 25°C and compound (LV) is formed in a quantitative yield. The aromatisation of (LV) to (LVI) takes place in concentrated sulphuric acid at temperatures below 0°C, in polyphophoric acid at 25 to 50°C, or when acted upon by gaseous hydrogen chloride or by hydrogen bromide in glacial acetic acid.

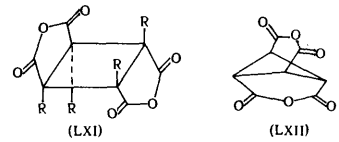
The use of α-phenylfuran or 5-phenylfurfural in the above reactions makes it possible to obtain tetracarboxylic acids with phenyl substituents in the ring of the phthalic acid group.

2. 2 + 2 Photocycloaddition Reactions

Until recently the application of the 2 + 2 photoaddition method for the synthesis of tetracarboxylic acids was restricted to the dimerisation of dimethyl fumarate and maleic anhydride and of their substituted analogues to form cyclobutane-1,2,3,4-tetracarboxylic acids. Among the four isomers of this acid, (LVII)–(LX), the first three are capable of forming the dianhydride and by virtue of this method all are known:

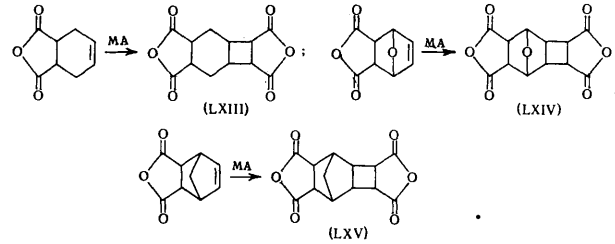


Irradiation at 253 nm of dimethyl fumarate in the solid phase, usually in the presence of a sensitiser, leads to the tetramethyl ester of (LVII) in the course of 7–8 days, which isomerises at 300°C to the thermodynamically more stable ester of (LVIII). [137] The hydrolysis of the esters and subsequent dehydration lead to the corresponding dianhydrides (LXI) and (LXII). [138] The dianhydride of the acid (LIX) was obtained by the ozonolysis of the acenaphthene dimer [76]. Irradiation of maleic anhydride under the same conditions leads directly [139] to compound (LXI, R = H):



The method is applicable also to methyl-, dimethyl-, and diphenyl-maleic anhydrides [139,140]. In this case, the reaction proceeds more readily. Dimethylmaleic anhydride dimerises to compound (LXI, R = CH_3) in 60% yield over a period of 6 h and the dimer (LXI, R = C_6H_5) is formed in a quantitative yield when the monomer is merely exposed to sunlight.

The scope of the 2 + 2 cycloaddition method was greatly extended recently in relation to the formation of dianhydrides [141]. The sensitised addition of maleic anhydride to tetrahydrophthalic anhydride and its 1,4-*endo*-*exo*- and 1,4-*endo*-methano-derivatives leads to the dianhydrides (LXIII)–(LXV):



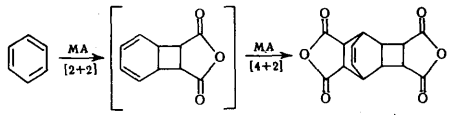
This method is particularly valuable because the initial compounds are very readily available—they are adducts obtained in the Diels–Alder reaction between maleic anhydride on the one hand and butadiene, furan, and cyclopentadiene on the other. Thus there is a possibility of using for the synthesis of dianhydrides a whole class of compounds—maleic anhydride monoadducts. The yield of compounds (LXIII)–(LXV) reaches 30–35%. [142]

The high thermal stability of the 2 + 2 photocycloaddition adducts is striking, this incidentally being in full agreement with theoretical postulates. Thus the dimer

of diphenylmaleic anhydride melts without decomposition at 325°C, the dianhydride of tetramethylcyclobutanetetracarboxylic acid decomposes above 350°C, and the adduct (LXIV) has a very high decomposition temperature for non-aromatic compounds (410°C, on fusion).

3. Successive 2 + 2 and 4 + 2 Cycloaddition Reactions

Irradiation of maleic anhydride solutions in benzene leads to the formation of a 2:1 adduct which has the structure of the dianhydride of tricyclo[4,2,2,$0^{2,5}$]dec-7-ene-3,4,9,10-tetracarboxylic acid (LXVI) according to chemical and physical data [143-145]. Since thermal 2 + 2 addition reactions are forbidden on symmetry grounds and benzene does not react with maleic anhydride in the dark even under very severe conditions, a process mechanism involving successive 2 + 2 and 4 + 2 cycloadditions was proposed [144]:



(LXVI)

It has been shown [144,146] that maleic anhydride and benzene form a charge-transfer complex absorbing in the range 230–280 nm, where the photochemical reaction takes place. Irradiation in the non-sensitised process activates the charge-transfer complex and not the species to be added, the activated intermediate being insensitive to oxygen, since it is in a singlet state [147]. Cycloaddition sensitised by aromatic ketones, for example benzophenone, involves energy transfer from benzophenone in the triplet state to the charge-transfer complex. The sensitised mechanism of the intermolecular energy transfer is more effective, although the sensitiser inhibits the reaction involving the non-sensitised addition mechanism. Acetone also behaves as a sensitiser and in addition plays the role of an active solvent [148].

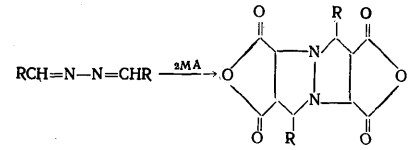
Apart from maleic anhydride, maleimide and its n-alkyl derivatives are capable of reacting with benzene. Among the *N*-aryl derivatives only those are involved in the reaction where the substituent at the nitrogen atom is not coplanar with the remainder of the molecule, for example the benzyl, *o*-tolyl, and 2,6-xylyl derivatives [149].

Many mono- and poly-substituted benzenes, naphthalene, and biphenylene have been employed as the aromatic component. In this group of compounds only monoalkyl- (methyl, ethyl, isopropyl, t-butyl, and C_3–C_{13} n-alkyl) and monohalogeno-benzenes, *o*- and *p*-xylenes, and biphenyl proved to be reactive [150-152]. All the substituents lower the rate of sensitised addition of maleic anhydride and the yield of products. If the rate of reaction of benzene is adopted as unity, then the rates are 0.5 for toluene, 0.25 for t-butylbenzene and chlorobenzene, 0.12 for biphenyl, 0.15 for *o*-xylene, and 0.08 for *p*-xylene [152].

From the practical point of view, the adduct of benzene and maleic anhydride is of greatest interest: it is obtained in the highest yield (70%) and has the highest melting point (350°C).

4. 1,3-Cycloaddition Reactions

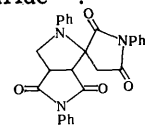
In view of the small number of examples of the application of this method for the synthesis of tetracarboxylic acids, we did not devote a separate section to reactions of this type, although the principle and mechanism of the 1,3-cycloaddition process are very different from those of the reaction discussed above. Haring and Wagner-Jauregg [153] showed that azines react with maleic anhydride via a 1,3-addition mechanism with formation of the dianhydrides (LXVII), in which R = H, phenyl, 2-furyl, *p*-chlorophenyl, *p*-methoxyphenyl, etc.:



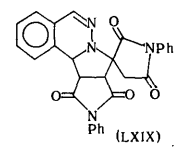
(LXVII)

When bismaleimides are employed instead of maleic anhydride, the azines can form polyimides [154].

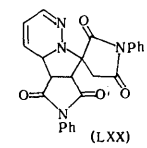
Schiff bases are also reactive in dipolar addition reactions with many maleic acid derivatives. Benzylidenemethylamine reacts with *N*-phenylmaleimide to form the spiroadduct (LXVIII) [155] via an intermediate azomethinylide [156]. Similarly phthalazine and pyridazine form the 1:2 adducts (LXIX) and (LXX) with maleimide in very high yields [157], although previously a structure with condensed rings was proposed for the adduct of pyrazine and maleic anhydride [158]:



(LXVIII)

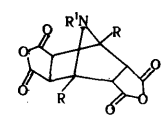


(LXIX)



(LXX)

Functional derivatives of tetracarboxylic acid (LXXI) with R = phenyl or *p*-methoxyphenyl and R′ = H or methyl were also obtained by the reaction of maleic anhydride or maleimides with azlactones or mesoionic azlactones—2,4-diphenyl-5-oxazolone, *N*-(*p*-methoxybenzyl)phenylglycine, and anhydro-5-hydroxy-3-methyl-2,4-diphenyloxazolium hydroxide [159]. The reaction is carried out by 1,4-cycloaddition methods and the products are obtained in an almost quantitative yield.



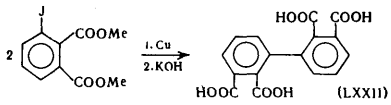
(LXXI)

IV. CONDENSATION OF DICARBOXYLIC ACIDS AND THEIR DERIVATIVES

The methods of synthesising tetracarboxylic acids discussed in this section cannot strictly speaking be combined in a general group, since they involve the employment of a very great variety of reactions. However, in view of the general idea underlying these reactions—the employment of chemical transformations of dicarboxylic acids for the preparation of tetracarboxy-derivatives—we separated these procedures from section V below.

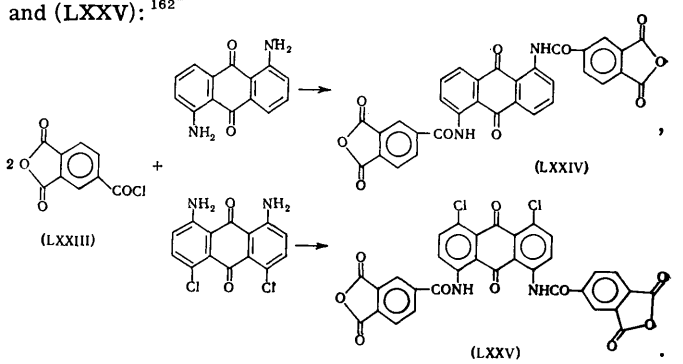
Reactions involving substituted phthalic acids are most often used for the synthesis of tetracarboxylic acids. Thus, when dimethyl 2-iodoisophthalate is heated at 240 to 250°C in the presence of powdered copper, tetramethyl biphenyl-2,2′,6,6′-tetracarboxylate is obtained [160]. The tetraester of biphenyl-2,2′,3,3′-tetracarboxylic acid was synthesised similarly from dimethyl 3-iodophthalate, the

free acid (LXXII) being produced by the hydrolysis of the ester[161]:



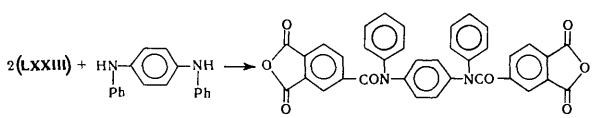
(LXXII)

Many tetracarboxylic acids specially designed for the synthesis of polymers have been obtained from trimellitic acid and its functional derivatives. The reaction of the chloride of the 1,2-anhydride of trimellitic acid (LXXIII) with 1,5-diaminoanthraquinone and 1,8-diamino-4,5-dichloroanthraquinone yielded the dianhydrides (LXXIV) and (LXXV):[162]



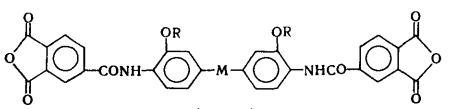
(LXXIII) (LXXIV) (LXXV)

The similar reaction of (LXXIII) with *NN'*-diphenyl-*p*-phenylenediamine leads to the dianhydride (LXXVI):[163]



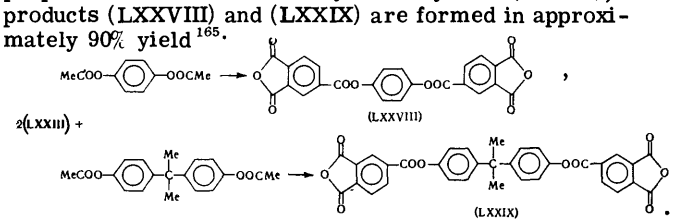
(LXXVI)

Seven dianhydrides with the general formula (LXXVII), in which R = alkyl and M = oxygen atom or a single bond, were obtained by the reaction of (LXXIII) with the hydrochlorides of di-(3-alkoxy-4-aminophenyl) ethers or 3,3'-dialkoxybenzidines[164]:



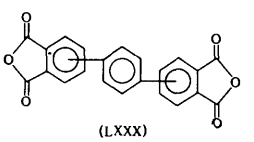
(LXXVII)

When *p*-diacetoxybenzene and 2,2-di-(*p*-acetoxyphenyl)-propane are transesterified by the anhydride (LXXIII), the products (LXXVIII) and (LXXIX) are formed in approximately 90% yield[165].



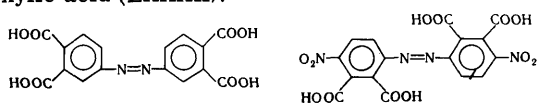
(LXXVIII) (LXXIX)

The reaction of *p*-di(chlorosulpho)benzene with phthalic anhydride has been patented as a method of synthesising a mixture of isomeric dianhydrides of terphenyltetracarboxylic acids (LXXX):[166]



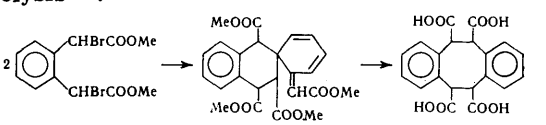
(LXXX)

The reduction of nitrophthalic acids constitutes a very convenient method of synthesising azobisphthalic acids. When *p*-nitrophthalic acid is treated with aluminium powder in an alkaline solution, azobenzene-3,3',4,4'-tetracarboxylic acid (LXXXI) is formed[167]. 3,6-Dinitrophthalic is reduced by glucose in the presence of sodium thiosulphate to 6,6'-dinitroazobenzene-2,2',3,3'-tetracarboxylic acid (LXXXII):[168]



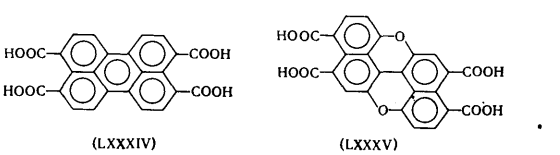
(LXXXI) (LXXXII)

On treatment with sodium iodide in DMF and further heating in boiling xylene, the ester of *o*-phenylenedi-(bromoacetic) acid gives rise to the acid (LXXXIII) after hydrolysis[169]:



(LXXXIII)

Only two examples of the dimerisation of the functional derivatives of naphthalic acid are known, but these reactions lead to very valuable products. By fusing the imide of naphthalic acid with alkalies in the presence of oxygen and subsequent hydrolysis with sulphuric acid, perylene-3,4,9,10-tetracarboxylic acid (LXXXIV) was obtained[170,171] and dehydrogenation of 3-hydroxynaphthalic anhydride in boiling nitrobenzene in the presence of copper(II) chloride yields the dianhydride of perixanthenoxanthene-3,4,8,10-tetracarboxylic acid (LXXXV).[172]



(LXXXIV) (LXXXV)

Certain reactions employed in the dimerisation method, particularly those involving trimellitic anhydride, have attracted attention by their flexibility: they make it possible to obtain many tetracarboxylic acids and their anhydrides with a wide variety of groups linking the anhydride rings. In certain cases this method permits a simplification of the synthesis of the acid.

Moreover its value lies in the fact that it allows one to synthesise compounds which cannot be prepared by other methods, for example azodiphthalic, perylenetetracarboxylic and perixanthenetetracarboxylic acids.

V. SYNTHESIS FROM DERIVATIVES OF ACIDS

Syntheses with malonic ester are very widely used to prepare aliphatic tetracarboxylic acids with both linear and cyclic structures. However, in this case the products are mainly compounds each of which contains two carboxy-groups at the same carbon atom, for example cyclohexane-1,1,3,3-tetracarboxylic acid. Such compounds are outside the scope of the present review.

There remain only a few examples of the synthesis of tetracarboxylic acids capable of forming stable dianhydrides and only the syntheses of ethanetetracarboxylic and ethylenetetracarboxylic acids constitute examples of the classical application of this method, while the preparation of other products involves additional decarboxylation, oxidation, etc. stages.

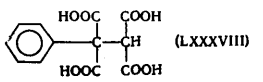
The interaction of bromo- and dibromo-malonic esters with sodium iodide leads to the tetraesters of ethanetetracarboxylic and ethylenetetracarboxylic acids from which the free acids (LXXXVI) and (LXXXVII) were isolated by hydrolysis [173]:

$$2\,CHBr(COOEt)_2 \xrightarrow{2NaI} (EtOOC)_2CHCH(COOEt)_2 \rightarrow (HOOC)_2CHCH(COOH)_2\ ,$$
(LXXXVI)

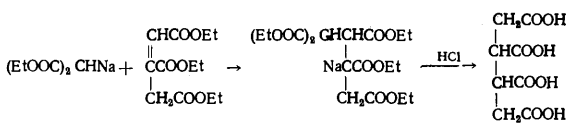
$$2\,CBr_2(COOEt)_2 \xrightarrow{2NaI} (EtOOC)_2C{=}C(COOEt)_2 \rightarrow (HOOC)_2C{=}C(COOH)_2\ .$$
(LXXXVII)

While treatment of compound (LXXXVI) with acetic anhydride leads smoothly to the dianhydride [174], the dianhydride of the acid (LXXXVII) is unstable and has not been isolated in a free state. However, being a powerful dienophile, it readily forms adducts with many dienes at the instant of its formation. Thus treatment of ethylenetetracarboxylic acid with acetyl chloride in the presence of 9,10-dimethoxyanthracene leads to the formation of its adduct with the dianhydride of the acid (LXXXVII). [89]

Treatment of (LXXXVII) with phenylmagnesium bromide yields phenylethane-1,1,2,2-tetracarboxylic acid (LXXXVIII): [175]

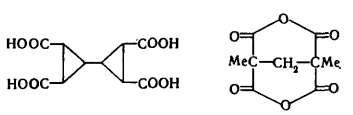

(LXXXVIII)

Butane-1,2,3,4-tetracarboxylic acid (LXXXIX) can be obtained by the reaction of sodiomalonic ester with aconitic acid ester [176,177]:


(LXXXIX)

The synthesis of dicyclopropyl-2,2',3,3'-tetracarboxylic acid (XC) also includes the decarboxylation stage [178]. The reaction of sodiomalonic ester and *trans,trans*-$CH_3OOCCCl{=}CHCH{=}CClCOOCH_3$ in methanol yields the hexamethyl ester of bicyclopropylhexacarboxylic acid, which gives rise to (XC) after hydrolysis and heating to 180°C.

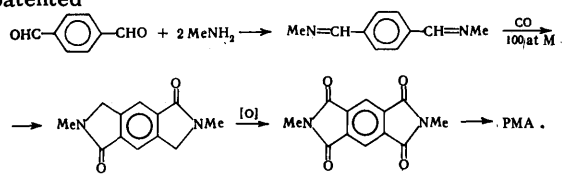
Pentane-1,2,4,5-tetracarboxylic and pentane-2,2,4,4-tetracarboxylic acids, (XCI) and (XCII), are also known. (XCI) has been obtained by the oxidation of the product of the reaction of malonic ester, methylene iodide, and sodium methoxide [179]. On treatment with diphenylketen, (XCII) is converted into the dianhydride (XCIII): [180]


(XC) (XCIII)

VI. SPECIFIC METHODS OF SYNTHESIS

In this section we shall consider methods of preparation of tetracarboxylic acids which are not general. However, all the examples described below satisfy one of three criteria: the method of preparation is specific, but the reaction product is of considerable interest; there is a prospect of further development of the method used at present to synthesise only one product; the method is used to synthesise many products, but the reaction mechanism has not been established.

The reactions involving the direct introduction of the carbonyl group constitute a familiar method of synthesising carboxylic acids, but it is applicable to the synthesis of only one tetracarboxy-compound—pyromellitic acid. A method of preparing pyromellitic acid by adding carbon monoxide to the Schiff base obtained from terephthalic aldehyde and methylamine and subsequent oxidation has been patented [181-183].

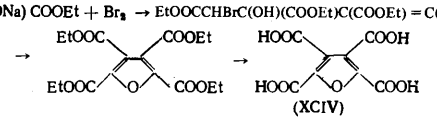


Pyromellitic acid is also formed in 35% yield on heating a mixture of sodium and potassium phthalates with calcium oxide and copper(II) chloride at a carbon dioxide pressure of 25 atm and 450°C. [184]

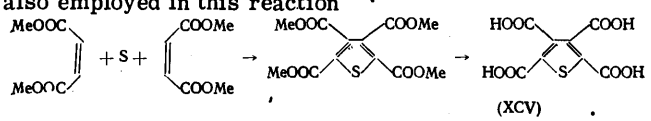
Of the tetracarboxylic acids which have already found practical applications, furan-, thiophen-, and dithiin-tetracarboxylic acids and the dianhydride of 1,2,5,6-bis-($\alpha\beta$-dicarboxypyrazino)anthraquinone were not described in the previous sections.

Furantetracarboxylic acid (XCIV) is formed on ring closure in tetraethyl dioxalylsuccinate—synthesised by treating with bromine the *O*-sodio-derivative of diethyl malate [185,186]. It has been shown [187] that the aldol $C_2H_5OOCCHBrC(OH)(COOC_2H_5)C(COOC_2H_5){=}C(ONa)COOC_2H_5$ is formed as an intermediate, splitting off subsequently NaBr and water with formation of (XCIV):

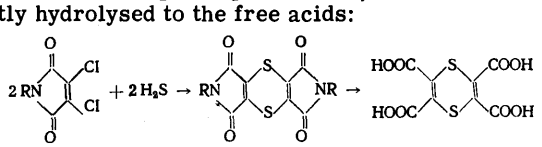
$$EtOOCCH{=}C(ONa)COOEt + Br_2 \rightarrow EtOOCCHBrC(OH)(COOEt)C(COOEt){=}C(ON_2)COOEt \rightarrow$$


(XCIV)

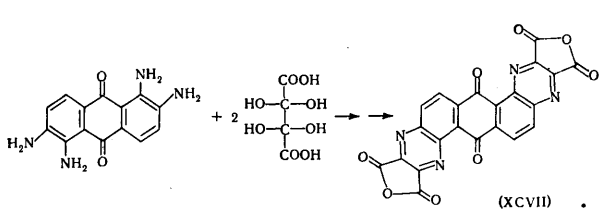
Thiophentetracarboxylic acid (XCV) was obtained initially by treating dimethyl acetylenedicarboxylate with sulphur [188] and later dimethylfumarate and maleate were also employed in this reaction [189].


(XCV)

Similar cyclisation reactions have been used to synthesise dithiintetracarboxylic acid (XCVI). [190] The interaction of dichloromaleimide with hydrogen sulphide or thiourea leads to the corresponding di-imides, which are subsequently hydrolysed to the free acids:

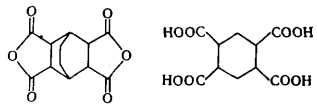

(XCVI)

The condensation of 1,2,5,6-tetra-aminoanthraquinone with dihydroxytartaric acid leads to 1,2,5,6-bis($\alpha\beta$-dicarboxypyrazino)anthraquinone, which cyclises to the anhydride (XCVII) on refluxing in acetic anhydride [191]:


(XCVII)

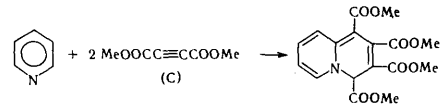
The dianhydride (XCVIII), which has a very high thermal stability, was obtained[192] by oxidising the adduct of dimethyl acetylenedicarboxylate and 7,8-diacetylbicyclo[4,2,0]octa-2,4-diene—the product of the intramolecular cyclisation of cyclo-octatetraene.

The Michael reaction has been used to synthesise a tetracarboxylic acid. The dehydrobromination product of trimethyl 1-bromopropane-1,1,2-tricarboxylate yields on treatment with sodium methoxide in methanol the hexamethyl ester of cyclohexane-1,1,2,4,4,5-hexacarboxylic acid, which is decarboxylated to cyclohexane-1,2,4,5-tetracarboxylic acid (XCIX) on refluxing with concentrated hydrochloric acid[193]:



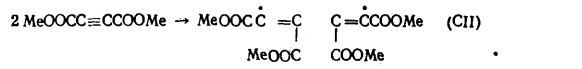
(XCVIII) (XCIX)

The adducts of pyridine with dimethyl acetylenedicarboxylate (C) [195,196] constitute a whole class of heteroaromatic tetracarboxylic acids, the first example of which was obtained by Diels[194]. Formally the reaction consists in the addition of two molecules of (C) to one molecule of pyridine with formation of the adduct (CI):



(C) (CI)

Diels proposed a mechanism for the process involving the formation of a dimer (C):



(CII)

Next compound (CII) attacks the nitrogen atom of pyridine via the positively charged centres and the intermediate is cyclised. If this mechanism were confirmed, the reaction could be classified as an example of diene synthesis, albeit of an unusual type. However, compound (CII) has not been detected by either chemical or spectroscopic methods. It is only known that the reaction at 20°C gives rise to 9*H*-quinolizine, which on heating isomerises quantitatively to the thermodynamically more stable 4*H*-isomer.

Many tetracarboxy-compounds based on substituted pyridines as well as quinoline, isoquinoline, acridine, and phenanthridine have been synthesised by this method. The tetramethyl esters are normally hydrolysed to the free acids, but the preparation of the dianhydrides has not been described.

VII. PRINCIPAL APPLICATIONS OF TETRACARBOXYLIC ACIDS

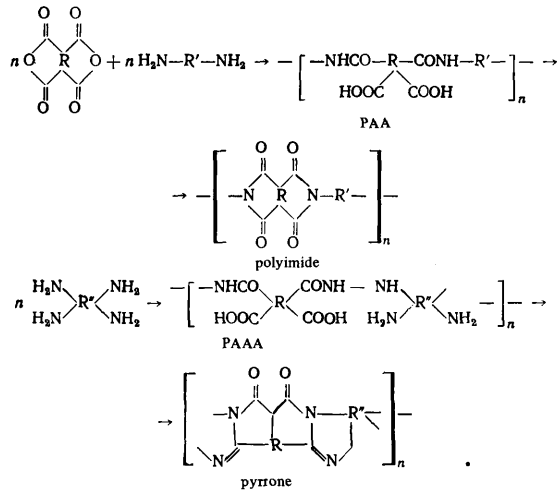
The first practical application of tetracarboxylic acids was discovered in the synthesis of dyes. The principal advances in this field are associated with the employment of the products of the condensation of naphthalene-1,4,5,8-tetracarboxylic acid and its substituted derivatives with aromatic *peri*- or *o*-diamines. The best known are Indanthren Bordeaux RR, Indanthren Brilliant Orange GR, and Indanthren Scarlet GG, which are respectively the *cis*- and *trans*-isomers of naphthoylenebisbenzimidazole and their mixture. These dyes are very stable, brillant, and have attractive tints[5].

Initially aroyleneimidazole dyes were used in vat-dying but in recent years they attracted considerable interest as disperse dyes for the dyeing of artificial fibres and Indanthren Scarlet GG and Indanthren Bordeaux RR were used to dye cotton.

Many dyes have been obtained on the basis of perylenetetracarboxylic acid (mainly di-imides) [197-199] and pyromellitic acid (benzoylenebisbenzimidazoles) [200].

The reactions of the dianhydrides of tetracarboxylic acids with diamines have been used to synthesise polyimides and the products of their reaction with *peri*-, *peri*- or *ortho*-, and *ortho*-tetramines are poly(aroylenebisbenzimidazoles) (pyrrones).

The polymers are formed via intermediate polyamidoacids (PAA) or polyaminoamidoacids (PAAA), which are then subjected to intramolecular cyclisation[1,2]:



PAA

polyimide

PAAA

pyrrone

The prepolymers (polyamidoacids, or polyaminoamidoacids), are made into articles by a two-stage method and are then subjected to solid-phase dehydration. In the one-stage method the mixture of components is heated to approximately 200°C in polyphosphoric acid or another solvent promoting dehydration, the intramolecular cyclisation processes being largely complete in the polymer isolated.

In the present review there is no need for a detailed analysis of the influence of the structure of the initial tetracarboxylic acid on the properties of the polymers, since these problems were discussed previously[1,2]. We shall only mention certain important characteristics.

The number of atoms in the anhydride rings of tetracarboxylic acids greatly influences the properties of the resulting polymers. This is due to the fact that the thermal stability and also many physicomechanical properties of polyimides and pyrrones are determined by the degree of completion of the intramolecular cyclisation processes. As stated above, in cyclisation the number of atoms in the resulting heterocycle is the same as in the initial dianhydride and therefore the degree of cyclisation in polymers based on six-membered dianhydrides, for example the dianhydride of naphthalene-1,4,5,8-tetracarboxylic acid, is higher and the resulting heterocycles are more stable than in the synthesis where five-membered dianhydrides, for example pyromellitic dianhydride, are employed [201-203].

The majority of polyimides and pyrrones have been obtained from aromatic dianhydrides and aromatic diamines or tetramines. Powerful intramolecular interactions,

which have a favourable effect on the thermal stability of the polymers but at the same time give rise to a poor solubility and absence of fluidity up to the decomposition temperature, are characteristics of such structures. It is fairly difficult and sometimes impossible to make such polymers into articles, so that usually one employs a two-stage method of synthesis with isolation of a soluble prepolymer, although this procedure suffers from a number of fundamental disadvantages [204]. On the other hand, it is known [204,205] that the introduction of bulky side groups into the polymer chain prevents close packing of the macromolecules and improves the solubility of the polymer. The employment of this procedure in the synthesis of polyimides and pyrrones, involving the use of the dianhydrides of aromatic tetracarboxylic acids containing phenyl, naphthyl, phthalide, fluorene, and other groups as substituents, permitted the synthesis of polymers capable of being made into articles when dissolved in organic solvents [206,207] without an appreciable decrease of their thermal stability.

Many methods of synthesising tetracarboxylic acids have been devised specially in order to obtain the starting compounds for the synthesis of polyimides and pyrrones. One may quote as examples the method for the preparation of adducts of maleic anhydride with caccyclones or coumalins [208], bisfuran derivatives [209], and benzene and its derivatives [210-212], the photoadducts with tetrahydrophthalic acids [3], and almost all the tetracarboxylic acids obtained by the oxidation of organic compounds and the condensation of dicarboxylic acids.

In the majority of studies dealing with the synthesis of new tetracarboxylic acids, it was stated that their dianhydrides were intended for the hardening of epoxy-resins and the preparation of plasticisers—the products of condensation with alcohols—in addition to the synthesis of polymers. However, few data have been quoted on the reactivity of the dianhydrides in these reactions and on the properties of the products.

Pyromellitic dianhydride is known [4] to be sparingly soluble in epoxy-resins and gel-formation takes place before complete dissolution of the dianhydride. On the other hand, a method has been discovered for the hardening of epoxides by the dianhydride of benzoquinonetetracarboxylic acid and its alkyl derivatives [213], whereby it is possible to raise the temperature of the onset of deformation to 288°C. The photoadducts of maleic anhydrides with ethylbenzene, cumene, and branched C_5–C_6 alkylbenzenes are highly compatible with epoxy-resins and the hardened products have very satisfactory mechanical properties, particularly at elevated temperatures [214].

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Institute of Chemical Physics,
USSR Academy of Sciences,
Moscow

U.D.C. 547.918

Biocatalysis of the Hydrolysis of the Glycosidic Linkage under the Influence of Lysozyme

V.I.Maksimov

As a result of the advances in the X-ray diffraction analysis of enzymes, it has recently become possible for the first time to describe in a concrete form and quite unambiguously the effective factors in biocatalysis. These factors have been demonstrated by means of biochemical, physicochemical, and physical research techniques. Lysozyme is the first enzyme for which such research has been carried out on an adequate scale. This review deals in fact with such investigations. The ultimate result was not only the solution of the problem of the specific mechanism of the action of this enzyme but also the broad outlines of the mechanisms of biocatalysis were finally established in principle. Instead of the old more or less probable hypotheses, these studies led to quite definite ideas about the mechanism of biocatalysis.
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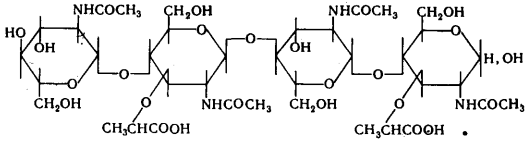
I. INTRODUCTION

Complete data on the X-ray diffraction analysis of lysozyme and its enzyme–substrate complexes with carbohydrates were published in 1967, the resolution being 2 Å.[1] At that time it was the only structure of an enzyme–substrate complex investigated in all details. It became possible for the first time to obtain for a specific example unambiguous data concerning the structure of the active centre and to put forward on the basis of these direct results a hypothesis about the mechanism of the action of the enzyme.

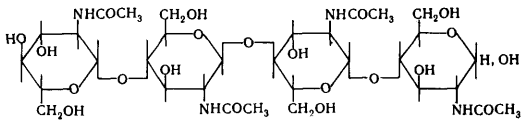
Chemical and physicochemical studies, which developed particularly vigorously after the above publication[1], made it possible to compare the structural data with the catalytic properties of the enzyme and the mechanism of the action of lysozyme has now been elucidated in broad outline. This example is instructive in many respects. Firstly, it shows that a problem as complex as an unambiguous description of the specific mechanism of the action of an enzyme can be solved only as a result of a combined study by various methods: chemical, biochemical, physicochemical, and physical. Secondly, it confirms the earlier view that the usual principles of physical organic chemistry underly the mechanism of biocatalysis. Thirdly, it demonstrates that the effective occurrence of a chemical process (biocatalysis) can be ensured not only by the direct action of the enzyme on the substrate linkages being dissociated but also as a result of a complex reaction pathway via intermediates, each of which is itself a substrate of lysozyme. The aim of the present review is to describe the chemical mechanism of the action of lysozyme and to show how complex the mode of interaction of the individual factors in biocatalysis can be and to attempt thereby to establish its fundamental essential features.

II. THE EARLY PERIOD IN THE STUDY OF THE ACTION OF LYSOZYME

Lysozyme became widely known as a result of Fleming's publication in 1922 describing the bacteriolytic action of a number of biological liquids and extracts[2]. Nothing was known for a long time about the chemical nature of lysozyme. A number of studies established that lysozyme can act on the polysaccharide components of cells with liberation of *N*-acetyl-D-glucosamine[3–5]. The chemical nature of the lysozyme substrate was definitely established for the first time by Berger and Weiser[6], who showed that chitin may be hydrolysed by lysozyme with formation of *N*-acetyl-D-glucosamine. It was thus shown that the lysis of bacteria takes place as a result of the hydrolysis of the polysaccharide at the β-(1–4)-glycosidic linkage connecting the *N*-acetyl-D-glucosamine residues. The first reports on low-molecular-weight substrates appeared in 1959–1960.[7–10] Salton and Ghysen[7,8] isolated a tetrasaccharide from the products of the lysozyme hydrolysis of bacterial cell walls and showed that the action of lysozyme on this substrate results in only one product—*N*-acetyl glucosamino-β(1–4)-*N*-acetyl muramic acid—a disaccharide the structure of which was finally established later[11,12]. The initial tetrasaccharide has the following structure:



The structure of another tetrasaccharide substrate, a fragment of chitin, is



The structure of the carbohydrate chain in the two cases is the same although the bacterial tetrasaccharide contains residues of D-lactic acid. Direct hydrolysis of the oligosaccharides was suggested in the above investigations[7-10] and also in later studies[13,14].

When lysozyme was allowed to act on a trisaccharide of similar structure, only two products were detected: a monosaccharide and a disaccharide[10,14]. According to Rupley[15], the glycosidic linkage is cleaved preferentially from the non-reducing end[15]. The first measurements of the rate of hydrolysis of oligosaccharides (chitin fragments) showed that the disaccharide is not hydrolysed by lysozyme at all, and the trisaccharide is hydrolysed very slowly, the rate of hydrolysis of oligosaccharides increasing with the length of the oligosaccharide[13].

III. THE MOLECULAR MECHANISM OF THE HYDROLYSIS OF SHORT OLIGOSACCHARIDES

The study of the mechanism of the action of lysozyme had two starting points. Firstly, it was established that short oligosaccharides are not hydrolysed directly, the reaction proceeding via the intermediate synthesis of longer oligosaccharides (hydrolysis via transglycosylation) and, secondly, it was shown that the hydrolysis goes almost completely to acetyl-D-glucosamine.

1. Hydrolysis via Transglycosylation

In 1964 Kravchenko and Maksimov[16] published the first report about the formation of high-molecular-weight water-insoluble products when lysozyme is allowed to act on various oligosaccharides derived from chitin. A similar phenomenon was observed by Sharon and Seifter[17], who employed a bacterial tetrasaccharide as the substrate. A number of communications confirming and extending the knowledge about the synthetic activity of lysozyme and showing that the formation of carbohydrates with a higher molecular weight proceeds via a transglycosylation mechanism (see, for example, Refs. 18–21) were published later.

It was possible to regard the transglycosylation reaction as a side process, which occurs under certain conditions (for example, at high substrate and enzyme concentrations). However, biochemical, X-ray diffraction, and physicochemical studies showed that transglycosylation is a fundamental intermediate stage in the hydrolysis of short oligosaccharides catalysed by lysozyme. Depending on the conditions, the process stops either at the stage of the total hydrolysis of the substrate to the monomer or at an intermediate stage.

The mechanism of hydrolysis via transglycosylation was formulated for the first time in 1965 by Maksimov et al.[19] The conclusion was based on the following experimental facts described for the first time in their report: (1) the induction period in the hydrolysis of short oligosaccharides; (2) the action of the seed†; (3) total hydrolysis of tri- and tetra-saccharides (involving all the glycosidic linkages). A trisaccharide is not split to the monomer and the dimer, as was believed by some investigators[10,14,15], but only to the monomer; (4) a change in the mode of reaction, towards hydrolysis or synthesis, depending on the concentrations, of the enzyme and substrate. Moreover, account was taken of the fact that the rates of the hydrolytic[13] and synthetic[16] lysozyme reactions increase appreciably with increase in the length of the oligosaccharide substrate. On the other hand, it was established that a trisaccharide cannot in principle be hydrolysed by lysozyme directly.

The hydrolysis of this substrate is a result of a complex process the mechanism of which was put forward in 1965:[19]

(1) short oligosaccharides

$$+\ \text{short oligosaccharide} \xrightarrow[\text{sylation}]{\text{transglyco-}} \text{long oligosaccharide} + \text{monomer (?)};$$

(2) long oligosaccharides

$$+\ \text{short oligosaccharide} \xrightarrow[\text{sylation hydrolysis}]{\text{transglyco-}} \text{long oligosaccharide} + \text{monomer (?)}.$$

hydrolysis

This scheme describes two reaction stages: the first is very slow, corresponding to the induction period in the course of which conditions are created for the second reaction stage. In the second stage the bulk of the substrate is digested, the process being cyclic. In a number of subsequent investigations[22-24] these findings were confirmed for other examples. The seed was regarded as a cofactor in the reaction, similar to a coenzyme[22]. It was shown that the substrate and the seed compete for the site where binding to the enzyme active centre takes place[24]. The study of the action of lysozyme on di-*N*-chloroacetylchitobiose showed that under certain conditions only one mole of monosaccharide is formed from one mole of disaccharide[23]. The following reaction mechanism was proposed[23]:

1. dimer + dimer → monomer + trimer;

2. dimer + oligosaccharide (x units) → monomer + oligosaccharide ($x + 1$ units).

According to this scheme, the first stage involves the formation of a seed by a disproportionation mechanism and in the second stage transglycosylation takes place mainly with formation of the monomer.

In 1967 Sharon published data showing that the bacterial tetrasaccharide hydrolyses only after an induction period, the duration of which is inversely proportional to the concentration of the enzyme[25]. Sharon also explains the observed lag period by the complexity of the hydrolytic process and by a molecular mechanism of the hydrolysis via transglycosylation.

In 1968 Chipman et al. published more detailed information about the molecular mechanism of the hydrolysis[26]. In their study the products formed when lysozyme was allowed to act on oligosaccharides from the *Micrococcus lysodeikticus* capsules were investigated by electrophoretic and paper chromatographic techniques and also by ion-exchange chromatography. The use of a tritium-labelled substrate permitted a simple solution of many aspects of the problem of the molecular mechanism. This study demonstrated convincingly that synthesis takes place mainly via a transglycosylation mechanism. The mechanism of the action of the seed was treated by analogy with a chain process, hexa- and octa-saccharides playing the role of the "chain carrier". In Chipman and Sharon's

† For the meaning of the term "seed" see Section IV, 3 (Ed. of Translation).

view[27], hydrolysis via transglycosylation is the most characteristic feature of catalysis by lysozyme. The study of the action of lysozyme on the glycosides of chitin oligosaccharides also led to this molecular mechanism. In 1968 the same view was adopted by Osawa[28] in a study of the hydrolysis of nitrophenyl glycosides of oligosaccharides and by Tsai et al.[29] in a study of the action of lysozyme on the glycosidic isologues of chitin disaccharides. Khorlin et al.[30] arrived at the same conclusion. A kinetic study of the molecular mechanism has been made[31].

2. Other Mechanisms

The molecular mechanism of the hydrolysis via transglycosylation has now been proved by many investigators[19,22-31]. However, many of them failed to take into account the fact in both earlier and later studies that the hydrolysis of chitin substrates does not take place directly[7-10,13,14]. The formation of transglycosylation products has been noted recently as a rule. However, the transglycosylation is regarded as a side reaction; assuming that hydrolysis and transglycosylation take place in parallel, Dahlquist and Raftery[32] reported in 1967 that, when lysozyme acts on tri-*N*-acetylchitotriose, a disaccharide and a monosaccharide are formed in molar proportions of 2 : 1 instead of 1 : 1 expected for direct hydrolysis. They suggest that part of the *N*-acetyl-D-glucosamine formed combines with the initial trisaccharide to produce a tetrasaccharide, which they detected among the reaction products. A similar mechanism was also put forward by Raftery and Rand-Mair[33], who believe that the formation of the β-methyl glycoside of *N*-acetyl-D-glycosamine, which they observed, is a result of a direct transfer of the acetylglycosamine residue from di-*N*-acetylchitobiose (the donor in the transglycosylation reaction) to methanol (the acceptor).

Rupley and coworkers also failed to take into account the necessity for the transglycosylation stage in the hydrolysis of short oligosaccharides[13,15,34]. Rupley and Gates considered a molecular mechanism according to which a productive complex of lysozyme and tri-*N*-acetylchitotriose is formed with an enzyme : substrate molar ratio of 1 : 2.[34] According to the authors, direct hydrolysis of one of the adsorbed trisaccharide molecules is then possible. Sharon and coworkers[26] regard such a mechanism as unlikely if only because two trisaccharide molecules contain one oxygen atom more than the hexasaccharide located in the active centre of lysozyme. Direct hydrolysis of tri-*N*-acetylchitotriose is also postulated in later investigations of Rupley and coworkers[35,36]. Rupley and Gates[34] attempted to determine the site of the dissociation of the glycosidic linkage in oligosaccharides in hydrolysis and transglycosylation assuming that the two processes occur in parallel. The reaction was performed with 0.001—0.05 M oligosaccharide and 0.1—0.8 M *N*-acetyl-D-glucosamine. In view of a large excess of *N*-acetyl-D-glucosamine (up to 1000-fold) the reaction must be restricted in this instance to transfer to the monomer. Some results of this investigation are presented in Table 1.

Table 1 shows that the rate of transglycosylation increases so much that the difference in rate for the dimer and hexamer is as much as 7 orders of magnitude. If one takes into account further the fact that, among the products of the reaction of the disaccharide with the monosaccharide in the presence of lysozyme, the authors observed at the end of the reaction a considerable amount of tri- and tetra-saccharides, the process in this system should presumably be self-accelerating owing to the increase of the reaction turnover with accumulation of longer oligosaccharides. Therefore, from our point of view, the mechanism of the cleavage of the dimer and trimer (and tetramer according to Sharon's data) presented in Table 1 corresponds to the induction period of the reaction.

Table 1. Characteristics of the cleavage of glycosidic bonds in chitin oligosaccharides in the reaction involving transfer to *N*-acetyl-D-glucosamine.

Oligosaccharide	Relative rate	Reaction order	Type of action
Dimer	0.003	1	
Trimer	1	1	$X_1\downarrow X_2\downarrow X_3$
Tetramer	8	1	$X_1\downarrow X_2\downarrow X_3\downarrow X_4$
Pentamer	4000	0	$X_1—X_2—X_3\downarrow X_4\downarrow X_5$
Hexamer	30000	0	$X_1—X_2—X_3—X_4\downarrow X_5—X_6$

In 1967 and 1969 Kravchenko and Kuznetsov published papers[37,38] describing the action of lysozyme on tetra-*N*-acetylchitotetraose. Together with all possible hydrolysis products, they observed the formation of a hexasaccharide the amount of which did not vary as long as the substrate remained, disappearing at the end of the reaction. On the basis of the content of hexasaccharide quoted in the figures and assuming it to be equal to 0.1 of an equivalent for the initial 8 equivalents of the tetrasaccharide, calculation of the ratio of the rates of transglycosylation (using the data of Rupley and Gates in Table 1) shows that the transglycosylation of the hexasaccharide should be 50 times faster, despite its low amount, than that of the tetrasaccharide (which behaves as the donor in this reaction). The authors suggest that the hydrolysis and transglycosylation take place simultaneously and the mechanism of hydrolysis via transglycosylation is not mentioned at all.

However, one should note that in certain cases short oligosaccharides can nevertheless hydrolyse directly. For example, the *p*-nitrophenyl glycosides of *N*-acetyl-*D*-glucosaminyl-D-glucose and *N*-acetyl-*D*-glucosaminyl-D-2-deoxyglucose can probably hydrolyse directly to disaccharides without the intermediate formation of longer oligosaccharides, as shown by appropriate techniques[39].

IV. THE CRYSTALLOGRAPHIC MODEL AND THE MOLECULAR MECHANISM

Fundamental and detailed data on the structure of enzyme—substrate complexes obtained by X-ray diffraction analysis appeared in 1967,[1] although some information had been published even earlier[40]. In these studies the complexes of lysozyme with various carbohydrates are referred to as enzyme-inhibitor complexes. This term probably arose as a result of the view, current at the time, that disaccharides are not substrates of lysozyme and trisaccharides hydrolyse slowly at concentrations corresponding to saturation (see Blake et al.[1], p. 385).

On the other hand, all these carbohydrates are capable of inhibiting the lysis of *Micrococcus lysodeikticus*. Recently the term "inhibitors", in relation to chitin or bacterial oligosaccharides, is used with decreasing frequency.

1. The Structural, Thermodynamic, and Functional Characteristics of the Binding Sites

Studies by English crystallographers have shown that the lysozyme molecule is a close-packed globule, close in shape to an ellipsoid of rotation with dimensions of $30 \times 30 \times 45$ Å. Across the globule, there is a deep cleft, which constitutes the active centre of the enzyme. In the formation of an enzyme–substrate complex, the carbohydrate is accommodated in the cleft; for each monomeric unit, there is a separate subsite—six in all. Consequently, the hexasaccharide molecule is capable of completely covering the cleft. Individual sorption subsites have been designated by the letters *A*, *B*, *C*, *D*, *E*, and *F*, starting with the subsite interacting with the non-reducing end of the hexasaccharide. Complexes with tetra-, penta-, and hexa-saccharides could not be detected by X-ray diffraction. The complex of lysozyme with a trisaccharide proved to be very stable and, moreover, the addition of the trisaccharide to the lysozyme did not affect the structure of the enzyme as a whole. Therefore, knowing the structure of lysozyme without the substrate, it was fairly easy to calculate the structure of this complex with the trisaccharide. It was found that the trisaccharide occupies subsites *A*, *B*, and *C* (*C* corresponds to the reducing end of the trisaccharide). Moreover, the retention of a certain rigidity by the enzyme structure on formation of its complexes with short substrates made it possible to obtain data concerning the structure of this enzyme–substrate complex too, by superimposing molecular models of the hexasaccharide onto the molecular model of lysozyme.

The very fact of the extrapolation of the structure of the enzyme–substrate complex to the *D*, *E*, and *F* subsites and confirmation of the validity of this extrapolation by all subsequent chemical and physicochemical data demonstrates quite clearly that the complementarity in the enzyme structure is not generated under the influence of the substrate but exists independently of the substrate. After the addition of the substrate to the lysozyme molecule, only insignificant structural changes take place. For example, a shift of the Trp 62 residue by 0.75 Å was noted.

Other residues also shift slightly, narrowing somewhat the cleft and giving rise to a closer contact between the enzyme and the substrate. However, an induced correspondence between the enzyme and substrate structures cannot be involved here. These changes in the enzyme structure can be more correctly regarded as an improvement of the existing complementarity in the interaction between lysozyme and the trisaccharide.

On the other hand, the substrate undergoes significant changes. Firstly, it loses the freedom of rotation about the C–O bonds joining the monomeric residues. Its structure becomes as rigid as that of the enzyme itself. Secondly, the rigid coupling of the enzyme to the substrate (hexasaccharide) forces the latter to alter the "chair" conformation of the pyrazine ring in one of the six subsites (*D*) and to assume a less stable and more strained "half-chair" conformation. This deformation of the structure of the carbohydrate unit at the *D* subsite is of decisive importance in catalysis by lysozyme. Measurement of the constants for the association of lysozyme with chitin and bacterial oligosaccharides by a wide variety of methods led to the determination of the energy of this interaction as the sum of the free energies of the interaction at all six subsites of the lysozyme molecule.

The results of these measurements are summarised in Chipman and Sharon's review[27] in the form of Table 2. The contributions $\Delta\Delta F_a^\circ$ introduced at each subsite separately are listed at the bottom of Table 2.

Table 2. Thermodynamic characteristics of the formation of enzyme–substrate complexes and of individual sorption subsites[27].*

Sorption subsite							ΔF_a^0, kcal mole^{-1}
X	A	B	C	D	E	F	
			NAG				−4.5(±0.3
		NAG	— NAG				−7.4
		NAM	— NAG				−7.9
	NAG	— NAG	— NAG				−9.2
	NAG	— NAM	— NAG				−9.8
	NAG	— NAM					⩾−4.2
	NAG	— NAM	— NAG	— NAM			⩾−6.9
	NAG	— NAM	— NAG	— NAM	—NAG	— NAM	−8.6
NAG	— NAG	— NAG	— NAG				−9.2
$\Delta\Delta F_a^0$, kcal mole^{-1}	0	−1.8	−2.9 ⩽−5.7	+2.9		−1.7	
			−3.4			(E+F)	

* NAG = *N*-acetyl-D-glucosamine; NAM = *N*-acetylmuramic acid.

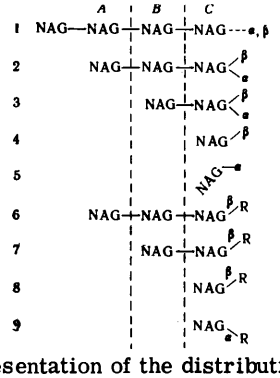
Table 2 shows that these contributions differ so significantly that they must be considered separately. The only subsite where there is a loss of energy is the *D* subsite, which can be readily explained by a change in the conformation of the carbohydrate residue at this site. On the other hand, the adjoining site is distinguished by the highest free energy gain, and hence the strongest binding of the substrate. According to data based on the crystallographic model, the sorbed *N*-acetyl-D-glucosamine is placed, as it were, in a hydrophobic "pocket".[41] In their paper dealing with the characteristics of the lysozyme complexes with various carbohydrates and related compounds, Rupley and coworkers[42] compared the free energies of formation of the lysozyme complexes with *N*-acetyl-D-glucosamine and *N*-methyl; *N*-hydroxyethyl-, and *N*-cyclohexyl-acetamides. They were found to be respectively −4.7, −2.4, −2.8 and, −3.1 kcal mole^{-1}. These and other data[42] show that the hydrophobic interaction of the acetamide group of the substrate makes a large contribution to the energy of formation of the complex. Thus a substrate with an *N*-acetamide group should always be sorbed in such a way that the *C* subsite is the first to be occupied.

It is readily seen that short chitin oligosaccharides (the dimer, trimer, and tetramer) should occupy subsites only to the left of *C* in Table 2. Phenomenologically this is shown by the finding that the affinity constant increases on passing from the monomer to the dimer and to the trimer, with very little change on further increase in the length of the substrate. The first quantitative data on this question were published by Dahlquist et al.[43], who obtained the following values for mono-, di-, tri-, tetra-, penta-, and hexa-saccharides: $(4-6)\times10^{-2}$, 1.75×10^{-4}, 6.58×10^{-6}, 9.45×10^{-5}, 9.35×10^{-6}, and 6.15×10^{-6}. The last two constants are only approximate, since even

before the attainment of equilibrium the substrates were partly hydrolysed. The data for the association constants of enzyme–substrate complexes obtained by different methods are presented in Chipman and Sharon's review[27]. The structures of the lysozyme complexes with chitin oligosaccharides and their glycosides have been investigated by NMR, which established the positions of all the residues[44].

In order to determine the positions of the remaining monomer units of the substrate in the active centre of lysozyme, measurements were made of the chemical shifts of the CH_3 protons of the acetamide groups of the chitin oligosaccharides in a free form and in their complexes with lysozyme. On formation of enzyme–substrate complexes, a shift of NMR signals towards higher fields and their broadening were observed. The acetamide groups of the chitin oligosaccharides acquire different magnetic environments on formation of the complex. This makes it possible to characterise each monosaccharide residue of the oligomer in terms of the corresponding resonance. The rule of the distribution of monomer units in the active centre of lysozyme was thereby confirmed. The *C* subsite is the first to be occupied and the remaining sites come into contact with the substrate in the following sequence: *B* first and then *A*. As shown above, this accommodation rule is fully consistent with thermodynamic characteristics. It is interesting that even the tetrasaccharide obeys this preferential accommodation rule. One of its residues is outside the region of the active centre and this disposition is more favourable, since accommodation at the *A*, *B*, *C*, and *D* subsites must lead to a loss of energy of 2.9 kcal $mole^{-1}$.

The situation involving bacterial oligosaccharides is somewhat more complex. According to X-ray diffraction data, the *N*-acetylmuramic acid (NAM) residue cannot be accommodated at the *A* and *C* subsites owing to steric hindrance[1]. For this reason, it is most probable that the NAG–NAM disaccharide is located at the *A* and *B* subsites, while the *C* subsite remains free.



Schematic representation of the distribution of *N*-acetyl-D-glucosamine (NAG) residues of oligosaccharides among the *A*, *B*, and *C* subsites of lysozyme[44].

As already mentioned, the last two subsites, *E* and *F*, were obtained by the extrapolation of X-ray diffraction data. They have been investigated experimentally much less satisfactorily. According to Sharon and coworkers[27,45], the long-lived glycosyl derivatives obtained by the elimination of the "aglycone" are located at the *A*, *B*, *C*, and *D* subsites, while the *E* and *F* subsites contain the acceptor molecules after the elimination of the aglycone residues. The formation of a lysozyme–acceptor complex cannot be recorded directly. However, this was achieved by a quantitative study of the products of the transglycosylation reaction[45]. Using as acceptors a mixture of two substances simultaneously, the authors inferred the proportions of the transglycosylation products formed from the relative rates of their formation. Comparison of two acceptors, glucose and *N*-acetyl-D-glucosamine, showed that hydrophobic interactions in the formation of the enzyme–substrate complex play an active role at the *E* subsite. Their contribution to ΔF can be estimated as -0.9 kcal $mole^{-1}$. It was discovered similarly that these interactions do not occur at the *F* subsite. Thus it was possible to estimate the overall contribution of the *E* and *F* subsites to ΔF, which is -1.7 kcal $mole^{-1}$ (Table 2). Evidently it is comparatively small and therefore, in order to drive the process towards transglycosylation, it is necessary that the acceptor concentration should be significantly higher than the donor concentration. The acceptor subsite of lysozyme as well as the donor subsite apparently do not undergo far-reaching changes on formation of the enzyme–substrate complex. Sharon and coworkers[46] tested 40 different monosaccharides and disaccharides as acceptors and showed that only those substances whose geometry corresponds to the surface of the *E* subsite may function as acceptors: only 29 acceptors were found. The remaining 11 substances are not complementary in relation to the *E* subsite and do not react at all. It is most interesting that a geometrical correspondence can be achieved by accommodating the acceptor in different ways. For this reason not only hexoses but also pentoses and even carbohydrates of the L-series can function as acceptors and the glycosidic linkages formed are not only of the β-(1–4) type but also of the β-(1–2)- and β-(1–3)- types. The reactivity of the acceptors could be predicted on the basis of data for the structure of the *E* subsite. For example, D-xylose can be accommodated at the *E* subsite in three ways, which correspond to the formation of products with 1–2, 1–3, and 1–4 glycosidic linkages[49].

2. Productive and Non-productive Enzyme–Substrate Complexes

The thermodynamic properties of the sorption subsites in the active centre of lysozyme account for the existence of the so called non-productive complexes. The very name "non-productive" complexes implies that the formation of such enzyme–substrate complexes does not lead to the dissociation or formation of covalent bonds. English crystallographers, who devised models of lysozyme, postulated that the dissociation of the glycosidic linkage in an oligosaccharide can take place only between units at the *D* and *E* subsites[1]. Further experimental studies confirmed this hypothesis and it is now generally accepted[27]. As shown above, the sorption of di-, tri- and tetra-saccharides take place preferentially at the *A*, *B*, and *C* subsites, i.e. outside the region of glycosidic linkages. Consequently all these complexes, the preferential formation of which is observed at substrate concentrations corresponding to saturation, are non-productive. For this reason, they were readily detected by X-ray diffraction analysis and a wide variety of physicochemical methods[27].

In order to form a productive complex, it is necessary to overcome the energy barrier associated with sorption

at the *D* subsite. It is readily seen that the barrier for oligosaccharides produced by the fragmentation of chitin can be overcome only as a result of the simultaneous coverage of almost all the sorption subsites in the lysozyme active centre. Productive complexes with such oligosaccharides can be obtained only with the hexasaccharide or possibly the pentasaccharide. This conclusion is proved, in particular, by the application of a competitive inhibitor such as the dye Biebrich scarlet[36], which is capable of being specifically sorbed in the region of the active centre. The affinity constants for the productive and non-productive complexes of tri-*N*-acetylchitotriose with lysozyme were determined with the aid of this inhibitor. They are respectively 1.0×10^{-2} and 1.5×10^{-5} mole litre^{-1}. The number of non-productive complexes formed is greater by almost 3 powers of ten than that of the productive complexes. The affinity constant for the productive complex of the hexasaccharide was estimated in this investigation as 5×10^{-6} mole litre^{-1}, which is very close to the affinity constant for the non-productive complex of the substrate.

Cases have been described where short oligosaccharides can form preferentially productive complexes. For example, *p*-nitrophenyl-4-O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-β-D-glucopyranoside can be slowly hydrolysed by lysozyme without complication by the transglycosylation reaction[39]. The carbohydrate residues of this disaccharide occupy the *C* and *D* subsites and the nitrophenyl glycosidic linkage is in the cleavage zone, which makes possible direct hydrolysis without transglycosylation. A similar result was obtained for trisaccharides with D-glucose, D-xylose, and D-galactose residues at the reducing end, the last being hydrolysed much faster than all others[47]. In this case too only a productive complex of the *CDE* type (*C* = NAG, *D* = NAG, and *E* = galactose) is probably formed.

3. Interpretation of the Molecular Mechanism

Without assuming the molecular mechanism of hydrolysis via transglycosylation, it is impossible to combine the data for the structural and thermodynamic characteristics of the sorption subsites of lysozyme. These characteristics and also the hypotheses concerning the productive and non-productive complexes of lysozyme with substrates which follow from them show that in the course of the enzymatic reaction a hexasaccharide or a longer oligosaccharide functions continuously on the surface of the active centre. It is either lengthened as a result of transglycosylation or shortened as a result of hydrolysis and the cyclic process ultimately results in the hydrolysis of the short oligosaccharide involved in the reaction in the transglycosylation stage as an acceptor. The presence of a small amount of a long oligosaccharide is necessary for the effective hydrolysis of short oligosaccharides, the long oligosaccharides behaving as the "seed" in the reaction.

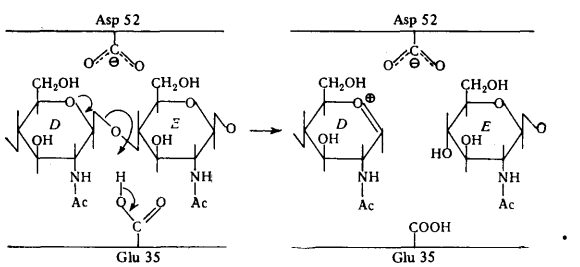
The degree of hydrolysis of the oligosaccharide depends on its structure. Chitin trisaccharides and tetrasaccharides are almost completely cleaved to the monomer[19], while the bacterial trisaccharide is cleaved only to the dimer[26]. This difference can be explained by the fact that the NAM residues in bacterial oligosaccharides cannot be accommodated at the *A*, *C*, and *F* subsites. Moreoever, the inhibiting action of the reaction product on the enzyme is more marked for a disaccharide than for a monosaccharide, since the former is sorbed more strongly.

V. THE ELECTRONIC MECHANISM

1. X-Ray Diffraction Data

Analysis of the structure of lysozyme complexes with substrates also makes it possible to put forward a hypothesis concerning the electronic-conformational principles of catalysis in this specific case. Investigators began with the assumption that the lysozyme complex with tri-*N*-acetylchitotriose (at the *A*, *B*, and *C* subsites), which they detected, is unreactive or non-productive. The complex which is undetectable by this method must be reactive. The most probable site of the dissociation of glycosidic linkages is between the *D* and *E* subsites. The only ionogenic groups located within the cleft and capable of participating in proton transfer are two carboxy-groups (the β-COOH group of Asp 52 and the γ-COOH group of Glu 35), which are located on either side of the β-(1—4)-glycosidic linkage of the substrate. The Glu 35 residue is located preferentially in the non-polar region near the bottom of the cleft, which must hinder the dissociation of the COOH group. Indeed, the pK_a values for these groups are about 6 while the usual value is 4.5—4.6. The Asp 52 residue is in the polar region and is linked by hydrogen bonds to amide groups which behave as proton acceptors. This facilitates the dissociation of the COOH groups of this residue. Their pK_a values are displaced to the acid region compared with the normal value (about 4 and about 4.5 respectively). Thus, by virtue of the rigid fixation of these functional groups and the formation of a stable microenvironment around each, they are ionised to different extents.

A second feature of the conformational-electronic mechanism of the action of lysozyme is the deformation of the glucopyranose ring at the *D* subsite. The stereochemical characteristics of the *D* subsites are such that the carbohydrate residue assumes the half-chair conformation. This is associated with energy consumption (see above), which is compensated by the binding energy at other sorption subsites. However, such deformation promotes the heterolysis of the glycosidic linkage, since it corresponds to a stable conformation of the carbonium ion. The role of the carboxy-groups in this process is that one of them (Glu 35) initiates the heterolysis of the glycosidic linkage, while the other (Asp 52) stabilises the intermediate cation. The mechanism of this process can be represented as follows:



The free carbohydrate residues are desorbed from the *E* and *F* subsites and the reaction is subsequently completed either by the addition of water (hydrolysis) or by sorption of other oligosaccharides at the *E* and *F* sites and the formation of a new glycosidic linkage (transglycosylation). Thus general acid catalysis obtains in the mechanism of the action of lysozyme.

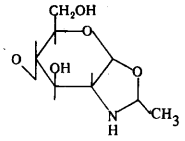
2. Chemical and Physicochemical Studies

Chemical and physicochemical studies should demonstrate the validity of the reaction mechanism put forward on the basis of structural data. Methods involving chemical modification of lysozyme established that the only groups involved directly in catalysis are the carboxy-groups[48,49]. The ϵ-NH_2 groups of the lysine residues, the terminal NH_2 group of lysozyme[43-50], the single histidine residue[50,52,54], the guanidino-groups of arginine[53], and the phenolic hydroxy-groups of tyrosine[50] can be completely blocked chemically without loss of the entire enzyme activity. In certain cases such modification led to a partial decrease of activity and in others to an increase[51,52,54]. The activity was determined as a rule turbidimetrically on the basis of the solvent action of the enzyme on a suspension of *Micrococcus lysodeikticus* bacteria. Naturally the dissolution of the bacterial suspension (lysis) is influenced by too many factors for a direct relation to be established between the quantitative changes in activity and structural factors. However, when it was possible to modify lysozyme at its carboxy-groups, a completely inactive derivative was obtained in many cases. The lysozyme molecule contains only 11 carboxy-groups (two glutamic acid residues, 8 aspartic acid residues and the *C*-terminal group). When the carbodi-imide method was used, it was possible to join to the carboxy-groups amino-derivatives such as $H_2NCH_2SO_3H$, $H_2NCH_2COOCH_3$, and $H_2NCH_2CONH_2$. One of the COOH groups of the active centre (Glu 35) cannot be amidated, while the other group (Asp 52) can be blocked, the substrate (trisaccharide) hindering the reaction[55,56]. The complete inactivation of the enzyme on blocking Asp 52 and the effect of the substrate on the reaction showed that this group is of critical importance for the activity. Similar results were obtained also on alkylation of lysozyme using triethyloxonium tetrafluoroborate as the alkylating agent[50,57]. This yielded a mixture of products, which was resolved by ion-exchange chromatography. Two monoalkylated lysozyme derivatives were isolated in a pure form, one of which was inactive but could be reactivated spontaneously at pH 2.0.[50] It was shown that this lysozyme derivative contains an alkylated COOH group of the Asp 52 residue[57]. The direct catalytic action of the carboxy-group of Glu 35 and Asp 52 is confirmed also by the finding that the blocking of all other carboxy-groups does not lead to complete loss of activity by lysozyme[55,56].

Both groups have unusual chemical properties. The Glu 35 residue is chemically inert although Lin and Koshland[56] claim that this group is sterically accessible for reaction. Ethyl-lysozyme (ethylated at Asp 52) also has unusual chemical properties. The ester linkage in this compound is incapable of involvement in nucleophilic substitution, is resistant to alkaline hydrolysis and the action of hydrazine and hydroxylamine, and is not reduced by $LiAlH_4$.[57]

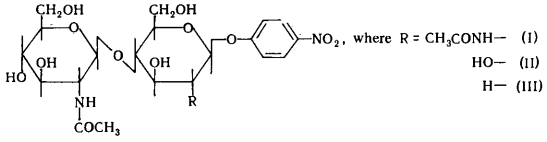
The mechanism of the chemical (non-enzymatic) hydrolysis of glycosides has been described in a review[58]. Therefore, it was natural to suppose that the carboxy-group of Glu 35 exhibits a catalytic activity via the mechanism of general acid catalysis. It protonates the glycosidic oxygen, which leads to the dissociation of the glycosidic linkage and the formation of a carbonium ion. As shown in the formula illustrated above, the dissociation of the glycosidic bridge at the C_1—O bond was demonstrated using water with the oxygen-18 isotope.

Raftery and Rand-Mair examined five probable electronic mechanisms of the cleavage of glycosidic linkages[33], two of which led to the formation of α-glycosidic linkages. These two mechanisms were rejected, since the authors showed that only the β-methyl glycoside of *N*-acetyl-D-glucosamine can be detected among the products of the reaction of di-*N*-acetylchitobiose with methanol. If the α-glycoside is in fact formed, its amount cannot exceed 0.3% in relation to the total content of methyl glycosides[59]. Consequently the reaction takes place with retention of the configuration at C_1 atom. Such a reaction could take place via Koshland's double nucleophilic substitution mechanism[60]. Moreover, there is a possibility of a mechanism involving the acetamide group (anchimeric cooperation) via a stage in which an oxazoline derivative is formed[61].



In experiments with model reactions, it was shown that the involvement of the acetamide group tends to accelerate the hydrolysis of the glycosidic linkage by a factor of 1000.[62] Finally, there is a possibility of a mechanism of the cleavage of the glycosidic linkage via a stage involving the formation of a carbonium ion, but with retention of the configuration at the $C_{(1)}$ atom owing to the oriented addition to the carbonium ion of the appropriate nucleophilic agent (water in hydrolysis or another acceptor in transfer).

For a final solution of this problem by a kinetic method, it is important to choose the substrate correctly, since the reaction investigated must proceed via a unique pathway. For this purpose, three substances of the type



were synthesised and it was shown that, when lysozyme acts on substance (I), a mixture of different carbohydrates is formed, while only the corresponding disaccharides could be isolated chromatographically from substances (II) and (III).[39] The association constant of the complex of lysozyme with (II) was determined by NMR (K_S = $1.5 \pm 0.3 \times 10^{-2}$ mole litre^{-1}) and it was found to agree satisfactorily with the Michaelis constant (K_m = $2.3 \pm 0.8 \times 10^{-2}$ mole litre^{-1}). Bearing in mind that the NAG residue in (III) is very strongly sorbed on the *C* subsite, one must conclude that (III) forms only a productive complex with lysozyme. This substrate was found to be most suitable for kinetic studies. The method of the secondary kinetic isotope effect (α-deuterium) was used for the solution of this problem[63]. Table 3 presents the characteristics of the secondary isotope effect for the hydrolysis of compound (III) under different conditions. Typical S_N2 reactions have rate constant ratios k_H/k_D of about unity (hydrolysis by sodium methoxide) and S_N1 reactions have a ratio of about 1.14 (hydrolysis by hydrochloric acid). Over a wide pH range, lysozyme has an isotope effect which corresponds to a considerable extent to an S_N1 reaction mechanism. For comparison, the authors investigated the mechanism of the hydrolysis of compound (III) catalysed by almond β-glucosidase and found that the

mechanism of the action of this enzyme is fundamentally different.

Lowe and coworkers[61,64,65] showed in a number of studies that the hydrolysis of oligosaccharides catalysed by lysozyme proceeds via the formation of an oxazoline derivative of the carbohydrate. They found that the kinetics of the hydrolysis of the *p*- and *o*- nitrophenyl glycosides of di-*N*-acetylchitobiose obey the Michaelis–Menten equation. However, despite the extensive investigations which they carried out, their conclusions concerning the involvement of the acetamide group in the catalytic reaction cannot be regarded as reliable, since in this instance the Michaelis–Menten equation was obeyed in a purely formal manner and lacked the physical significance usually attributed to it. In the study quoted above[63], it was shown that, when lysozyme acts on compound (I), a mixture of products is formed and that this substrate is unsuitable for kinetic studies on the electronic mechanism: therefore, the conclusions of Lowe and coworkers are groundless. The digestion of such substrate proceeds via a hydrolytic mechanism involving transglycosylation, as shown for nitrophenyl glycosides by Osawa[28]. The mechanism via the oxazoline derivative is also criticised in Chipman and Sharon's review[27].

Table 3.

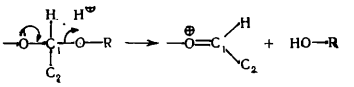
Conditions of hydrolysis	k_H/k_D
2 *N* HCl, 50°	1.13
3 *N* $NaOCH_3$, 70°	1.03
β-Glucosidase	1.015
Lysozyme	—
pH 5.5	1.11
pH 3.1	1.11
pH 8.3	1.11

3. Theory of Chemical Conjugation as One of the Preconditions for the Electronic Mechanism of the Action of Lysozyme

A characteristic feature of lysozyme catalysis discussed above is the obligatory action of the enzyme on the structure of the glucopyranose ring at the *D* subsite. Usually this is regarded as confirmation of the earlier hypotheses of the deformation and strain of the bonds undergoing dissociation on the surface of the active centre of the enzyme[1,27,58]. However, it is important to emphasise also the problem of the role of the conjugation of chemical bonds in biocatalysis. It is thereby possible to establish a relation between the classical concepts of organic chemistry and the concepts underlying the mechanism of biocatalysis.

The theory of bond conjugation and the effect of conjugation on reactivity were developed in organic chemistry a long time ago. One of the principal postulates concerning the conjugation of single bonds, which were developed by Nesmeyanov[68], is that specific stereochemical requirements must be met. The large class of organic reactions which occur as a result of the conjugation of single bonds, has been called "fragmentation reactions", which were studied on a wide scale both theoretically and experimentally by Grob and coworkers[68]. We have already mentioned that Grob's theory[67] of the fragmentation of organic substances is consistent in its main postulates with Nesmeyanov's theory of the conjugation of single bonds[66]. The differences between these theories concern mainly the terminology. Grob uses terms such as "stereoelectronic factor" and "frangomeric acceleration",[68,69] which reflect essentially the influence of molecular conformation on the reaction rate. It has also been suggested that the above frangomeric acceleration may be one of the factors in biocatalysis (Kossower[70]).

In the present author's studies on the fragmentation of α-aminoacids with a tertiary nitrogen atom, it was concluded that, by virtue of steric hindrance, the α-aminoacid molecule can assume a fixed conformation which is the most favourable for the conjugation of single bonds[71,72]. In this case the rotation in the aminoacid molecule about the N–C bond is hindered and the conformation is fixed in consequence of steric hindrance due to the bulky substituent at the nitrogen atom. The conformation of the substrate molecule is also fixed on formation of an enzyme–substrate complex. One cannot conclude that the fixation of the conformation is favourable for *p*, σ conjugation of the following type:



As a result of this conjugation, the transition state exists partly in the oxonium form with a double bond. The present author called this factor in biocatalysis "inclusion of conjugation" or the "steric-orientation factor".[73]

The molecular and electronic mechanisms of the action of lysozyme are interrelated. In order that the energy of the "chair–half-chair" transformation should be compensated by the energy of the formation of the enzyme–substrate complex, the involvement of six (or five) sorption centres is essential.

VI. CERTAIN UNSOLVED PROBLEMS

The study of the mechanism of the action of lysozyme constitutes an example of a combined investigation of a large research problem. For many reasons, lysozyme has proved convenient for study by X-ray diffraction. However, at the time of the completion of this review there were very few chemical and physicochemical data concerning the mechanism of its action on a substrate. Substrates with specific chemical characteristics became known only in 1960. The published X-ray diffraction data (1965–1967) on the structure of lysozyme and its complexes with substrates stimulated chemical and physicochemical research. In the course of approximately 5–6 years (1964–1969), almost all the details of the mechanism of the reaction of lysozyme were elucidated in a number of laboratories in the USSR, USA, England, Japan, France and other countries. The complete agreement between the chemical and physicochemical data on the one hand and the X-ray diffraction data on the other suggests that the mechanism of the action of lysozyme has been largely established correctly and fully.

However, there are still certain problems which require further investigation. These are related, in particular, to the nature of the structural changes in lysozyme in the pH range 6–7, which are reflected in its activity. The dissociation constants of both the imidazole group, the single histidine residue which is not involved directly in catalysis, and of the anomalous carboxy-group of Glu 35, which plays a key role in catalysis, have p*K*

values corresponding to the pH range. The dissociation of the carboxy-group, which occurs on increase of pH to 6—7 and above, is probably accompanied by changes in the details of the enzyme structure which increase the tendency towards aggregation of both native[74,75] and irradiated[76,77] protein in this pH range. It has been shown by NMR that the dimerisation of native lysozyme in solution takes place via the surface of the enzyme adjoining the region of the active centre[78]. The nature of the interaction of lysozyme with chitin is also obscure.

A detailed study showed in the first place that this interaction takes place as a result of a specific enzyme—substrate affinity. In the second place it was established that there exist two complexes between lysozyme and chitin, differing in a number of properties, particularly in the fact that one is formed preferentially at a pH below 6—7 and the other is formed under more basic conditions[79-82]. Since no other methods (differential ultraviolet spectroscopy, fluorescence, NMR spectroscopy, etc.) indicated the existence of two different lysozyme complexes with water-soluble substrates, the data obtained for the interaction of lysozyme with water-insoluble chitin can be interpreted as due to a characteristic feature of chitin itself, since, in contrast to low-molecular-weight and water-soluble substrates, chitin sorbs lysozyme molecules not only via an enzyme—substrate interaction but also as a result of forces acting on the interface between the solid (chitin) and liquid (solution) phases.

The study of the catalytic activity at high pH is also by no means complete. When lysozyme was allowed to act on *Micrococcus lysodeikticus* bacteria, it was noted that the dependence of the activity on the pH has a second maximum at pH 9.2.[83-85] Since it is unlikely that the carboxy-group of Glu 35 is protonated in this pH range, it was suggested that under these conditions general acid catalysis is not due to Glu 35 but to the ϵ-amino-group of Lys 97 located at the outlet from the cleft[84]. Later it was concluded[85] that the sorbed substrate (bacterial cell) affects the dissociation of Glu 35 in such a way that, owing to electrostatic interaction, it remains in an undissociated form even at pH 9.2. According to these data, tetra-*N*-acetylchitotetraose (an uncharged substrate) is not hydrolysed by lysozyme at pH in excess of 8.[85]

It has also been observed[86] that the pH optima for the hydrolase and transferase activities of lysozyme do not coincide: hydrolysis takes place preferentially at a lower pH and the synthetic activity is shown to a greater extent at an elevated pH (particularly at pH 8—9). The change in the type of catalytic activity of lysozyme on altering the pH may be attributed to the dissociation of the carboxy-group of Glu 35 and a correspondong change in the state of aggregation of the enzyme. The present author suggested[86] that the hydrolysis is due to the monomeric lysozyme molecule and transglycosylation is due to the dimeric molecule. One must emphasise that, over the entire region of the active centre, the *E* and *F* subsites have been most conclusively investigated; as stated above, the role of acceptor subsites is attributed to them.

However, the interrelations between the sorption of the substrate, catalysis, and the degree of aggregation of the enzyme, proved to be more complex than might have been expected. Many data show that the degree of activation of native[87-90] and irradiated[91,92] lysozyme is reduced in the presence of a substrate. Moreover, an impression has been created that the inhibiting action of the substrate on the dimerisation of lysozyme is shown even after its complete elimination. If this is so, the substrate induces structural changes in lysozyme, which persist for a long time[93]. In this case, one may be dealing with the so called subtle conformational changes. One should probably include among them those induced by the substrate at the opposite end of the enzyme molecule, which have been detected by the paramagnetic probe method[95].

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Lysozyme proved to be the first enzyme the most important details of the mechanism of whose action have been elucidated. It has also become clear that this mechanism cannot be extended to all related enzymes (glycosidases). Therefore, it is important to be able to isolate correctly the most general principles of biocatalysis constituting the basis of the mechanisms of the action of enzymes in general. In order to stay close to lysozyme, we shall consider as an example the hydrolysis of the glucosidic linkage. In order that the hydrolysis should follow the reaction pathway via the carbonium ion, it is necessary that (1) the glucosidic oxygen should be protonated, (2) that appropriate changes should occur in the conformation of the glucopyranose ring, and (3) that the negatively charged ion in the vicinity of the carbonium ion should assume an appropriate orientation. Each of the three conditions enumerated above is achieved with a certain degree of probability. The probability of the simultaneous coincidence of all three conditions is expressed by the products of the above three probabilities. We enumerated only the most important conditions responsible for the catalytic activity of lysozyme. In the general case the number of conditions may be even greater. The probability of the occurrence of a chemical reaction is equal to the product of the probabilities f_i of the occurrence of each condition:

$$f = f_1 \cdot f_2 \cdot f_3 \cdots f_n, \text{ where } f_i < 1$$

The greater the number of conditions involved in the mechanism of the process the smaller its overall probability. By altering the external parameters of the medium it is possible to achieve a sharp increase of the individual components of the probabilities f_i. For example, the hydrolysis of glycosides by acids implies a sharp increase of the probability of the protonation of the glycosidic oxygen (f_1) by collisions with protons (hydronium ions). An increase of temperature increases the probability of the occurrence of the transition state conformation (f_2). However, a simultaneous increase of the probabilities of the protonation (f_1) and orientation of the negative ion (f_3) in chemical systems is virtually unattainable. Only in certain individual cases, known as concerted action mechanisms, is this situation realised in non-enzymatic reactions. The familiar catalytic action of 2-hydroxypyridine on the mutarotation of glucose may serve as an example. This reaction is in fact usually regarded as one of the models of the enzymatic process. The orienting effect of the enzyme, which according to Koshland[96] ensures the mutual approach and appropriate orientation of the reacting sites in the substrate molecules, essentially reduces to an increase of the probability of occurrence of the conditions governing the transition state.

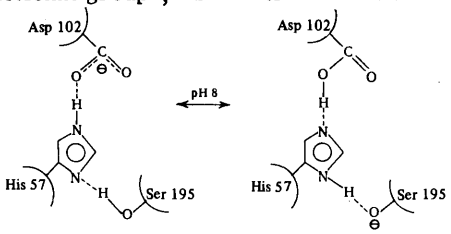
In lysozyme catalysis, the probability of each of the three conditions is very high, owing to the relatively rigid fixation of the "working" functional groups and their rigorous stereochemical correspondence to the substrate. A weak acid such as Glu 35 with $pK_a = 6—7$ protonates the glycosidic oxygen with the same high probability as, for

example, hydrochloric or sulphuric acid. The conformation of the transition state is determined by the stereochemical characteristics of the *D* subsite and its probability is probably very close to unity. The probability of the required orientation of the negative ion (of Asp 52) is just as high. The behaviour, which in a chemical process is a consequence of a random favourable combination of several conditions for the occurrence of the reaction, in an enzymatic process is programmed in the structure of the protein molecule. This in fact ensures a high efficiency of enzymatic catalysis.

The function of the enzyme is to organise the chemical process, drive it along a specific reaction pathway, and ensure a high probability of the necessary reaction conditions. This directing influence of the enzyme is possible only if the enzyme itself has a fairly rigid fixed structure. In low-molecular-weight compounds the rigidity of structure can be achieved mainly via covalent bonds, as, for example, in polycyclic steroid systems. In high-molecular-weight compounds the rigidity of structure is ensured by the compact packing of the polypeptide chain into globules and by non-covalent interactions. X-Ray diffraction analysis has shown that a wide variety of proteins have a close-packed globular structure with rigidly fixed positions of the polypeptide chains[97]. Therefore, when one speaks of the induced correspondence between the enzyme and the substrate, widely known as Koshland's hypothesis, such induction must be restricted to very small displacements of the atoms in the enzyme molecule. In lysozyme these shifts do not exceed a distance of 1 Å. Such slight structural changes in the protein can hardly serve as an adequate basis for the assertion of conformational flexibility, particularly since deformations of valence angles and distances are usually involved and not conformational changes.

The high molecular weight of the enzyme and its compact and rigid globular structure ensure the fixation of the individual functional groups, which leads to the appearance of new properties and phenomena unknown in organic chemistry. As a result of their fixed position, these groups remain in an almost unchanged microenvironment and their properties depend sharply on each specific microenvironment. In organic chemistry the functional group of any molecule is subject to the influence of a constantly varying microenvironment and the properties observed experimentally are as a rule macroproperties averaged with respect to the properties of the numerous microenvironments of the given group. Moreover, as a result of the fixation of the functional group in the rigid globule of the enzyme, there is also a possibility of the formation of structures which are unusual for organic chemistry. The above ideas can be illustrated by a number of examples.

The Asp 52 residue in the lysozyme molecule is fixed in a zone of enhanced nucleophilicity. It can be readily esterified by triethyloxonium tetrafluoroborate, but the resulting ester does not enter into nucleophilic substitution reactions (see above). The serine hydroxyl, which enters into the active centre of chymotrypsin, has unusual chemical properties. In this instance the enzyme exhibits a type of conjugation of chemical bonds which is unknown in organic chemistry. It would probably be correct to call it transannular conjugation, since it resembles most closely the transannular interaction in macrocyclic compounds. As a result of the rigid fixation of the functional groups in chymotrypsin, the geometrical disposition of Asp 102, His 57, and Ser 195 ensures chemical conjugation of their functional groups, as illustrated below:



The His 57 and Asp 102 residues are immersed in the globule and are not in contact with the solution. The Ser 195 residue projects onto the surface. As a result of this conjugation, the usual aliphatic hydroxy-group is capable of dissociation at pH 8, i.e. as regards this property it resembles the hydroxy-group of nitrophenol. As in catalysis, the probability of transannular conjugation in a mixture of the above three aminoacids is negligibly small, whereas in a protein it occurs with a probability of unity as a result of steric proximity.

The chemistry of proteins provides in addition examples of unusual structural formations. For instance, in lysozyme crystals one of the contacts between neighbouring enzyme molecules has a structure resembling the sandwich structures familiar in the chemistry of organometallic compounds. This structure is formed with participation of the benzene ring of phenylalanine in one lysozyme molecule and the phenolic ring of the tyrosine residue in another molecule. The guanidino-group of arginine in the form of a cation linked to a Cl^- anion is located between the parallel rings. Such a structure is stabilised by additional hydrogen bonds.

Biocatalysis is merely a special manifestation of the characteristics of the chemistry of proteins arising by virtue of their organised and almost time-invariant molecular structure.

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All-Union Institute of
the Biosynthesis of
Protein Materials,
Enzyme Division,
Moscow

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Semi-empirical Quantum-mechanical Methods for the Calculation of Molecular Geometry and Conformational Energies

V.G.Dashevskii

The LCAO-MO approximation is considered in the Hartree-Fock problem for many-electron systems, and Roothaan's equations are given, various "simplifications" of which form the foundation for most current semi-empirical methods for calculating the electronic structure of polyatomic molecules. Accounts are given of the most popular semi-empirical schemes enabling the geometry of a molecule to be predicted and several related properties—conformational energies, barriers to internal rotation, and energies of formation—to be calculated. The possibilities and limits of application of these methods are discussed. A list of 171 references is included.

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I. INTRODUCTION

The geometry of the ground state of a molecule is not only of purely structural interest but also, in the broad sense of the word, of chemical interest. Indeed, the thermochemical properties of molecules—differences in energy between rotational isomers, barriers to internal rotation, and heats of formation, hydrogenation, and structural isomerisation—are related to their geometry; frequencies of the vibrational spectra of polyatomic molecules, absorption in the microwave range due to transitions from one rotational level to another, and even electronic spectra are directly dependent on geometry; and finally the effect of the steric factor in reactions, especially organic, is only rarely negligible. Hence it is not surprising that calculations of molecular geometry, conformations, and the energies associated with confirmational transitions occupy an important place in current theoretical investigations.

The present Review covers calculations of bond lengths, valency angles, and conformations, mainly of polyatomic organic molecules. If a method is available for calculating the total energy of a molecule, the equilibrium geometry will clearly correspond to an absolute minimum in the total energy expressed in terms of independent geometric variables, in particular bond lengths, valency angles, and angles of rotation. The total energy surface may have not one but several minima, which, when they appear with variation of angles of rotation about bonds, are claimed to correspond to stable conformers. The difference in energy between conformers determines their

equilibrium in the gas phase (when interactions between molecules can be neglected). Saddle-points in the total energy surface, encountered on the way from one minimum to another, correspond to barriers to internal rotation or inversion, which are measured by various physicochemical methods.

Until the mid-1960s almost the sole method for calculating geometry and conformational energies was the classical model of a molecule, in which the potential energy is regarded as the sum of several contributions—deformation energies of valency bonds and angles, torsional stresses, etc.—and which has several names—the mechanical model of a molecule, the molecular force field model, and the Hill–Westheimer–Kitaigorodskii–Hendrickson–Wiberg model—the last name indicating the workers who have made the most significant contribution to the creation and development of the model[1-5]. The mechanical model has been used for numerous calculations of the conformations of organic molecules (see reviews[6-8]), macromolecules, and biopolymers[9-12], as well as energies of formation of molecules from atoms[13-15], vibrational frequencies in the spectra of polyatomic molecules[16,17], etc. Without doubt this simple model will for a long time yet be a powerful tool in the hands of physical chemists: it may be just as necessary in the present stage of the development of theoretical chemistry as three-dimensional models of molecules were necessary fifteen years ago (when methods of calculation were in a rudimentary state). It must be borne in mind, however, that a mechanical model of a molecule cannot be rigorously based on the fundamental laws of physics: it does not follow directly from the Schrödinger equation, and its constants are chosen by a purely empirical procedure. Although the predictive power of this model is very great, the fact that the nature of the interactions between electrons and nuclei is concealed in empirical constants often leaves a feeling of dissatisfaction.

Quantum-mechanical methods of calculation—both semi-empirical and non-empirical (calculations *ab initio*)—have become widespread during the past decade. This is due primarily to the creation of effective algorithms for evaluating quantum-mechanical integrals, to the elaboration of new semi-empirical methods, and finally to the development of computational technique (though electronic computers are required also for calculations based on the mechanical model) and the founding of the International Exchange Fund for Programmes on Quantum Chemistry. Quantum-mechanical methods are based on seeking approximate solutions of the Schrödinger equation, with many integrals neglected in semi-empirical methods, while many are parametrised by means of experimental data. Of course, calculations *ab initio*, in which no constants other than the fundamental physical constants—e, m, and h, (the charge and mass of the electron and Planck's constant)—are used, are preferable from any point of view, but the rapid action and the memory of present-day computers enable such computations to be made only for relatively simple molecules. Hence the need to work out semi-empirical methods, enabling results of importance for the chemist to be obtained with a relatively short machine time and by means of not very complicated programmes.

II. ROOTHAAN'S EQUATIONS AND POSSIBLE MODES OF "SIMPLIFICATION"

The non-relativistic "electronic" Schrödinger equation for a molecule containing N electrons can be written

$$H\Psi = E\Psi, \qquad (1)$$

$$H = \sum_{i=1}^{N} -\frac{1}{2}\nabla_i^2 - \sum_{i=1}^{N}\sum_{\alpha} Z_\alpha/R_{\alpha i} + \sum_{i=1}^{N}\sum_{j=i+1}^{N} 1/r_{ij}, \qquad (2)$$

where $\Psi \equiv \Psi(x_1, x_2, \ldots, x_N)$ is the wave function depending on the spatial and spin coordinates x_i of the electrons, E is the energy, and H is the electronic Hamiltonian, representing the sum (2) of the kinetic energy operators of the electrons, the potential energy of attraction of electrons to nuclei, and the potential energy of mutual repulsion of the electrons. Atomic units in which $m = e = h = 1$, have been used in Eqn. (2): the eigenvalues obtained for the energy operator H will then also be expressed in atomic units or hartrees (1 a.u. $\equiv$ 1 hartree = 27.210 eV = 627.46 kcal mole^{-1}). Furthermore, Z, R, and r in (2) denote respectively the charge on the nucleus, the distance between electrons and nucleus, and the distance between electrons; the subscripts i and j refer to electrons, and the subscript α indicates nuclei; and ∇_i^2 is the Laplace operator for the ith electron.

The electronic Schrödinger equation emerges in the Born–Oppenheimer approximation, according to which the motions of electrons and nuclei in a molecule can be regarded with sufficient accuracy as independent. In order to obtain the total energy of the molecule, however, the eigenvalue E of the electronic equation (1) must be supplemented by the potential energy of repulsion of the nuclei V_{nn}, which is given by the formula

$$V_{nn} = \sum_{\alpha}\sum_{\beta(\neq\alpha)} Z_\alpha Z_\beta/R_{\alpha\beta}, \qquad (3)$$

where the subscripts α and β refer to nuclei. Thus the Born–Oppenheimer approximation enables the problem of the quantum-mechanical calculation of a molecule to be solved with fixed nuclei, their interaction being taken into account only after the "electronic" calculation.

The difficulty in solving Eqn. (1) with the Hamiltonian (2) is due mainly to the large number of independent variables and the presence of terms of the form $1/r_{ij}$. The model of independent electrons (the Hartree–Fock model) permits considerable simplification of the problem, by introducing for each electron the mean potential V_i produced by the other electrons and the nuclei. Instead of (2) we can then write

$$H = \sum_{i=1}^{N}\left[-\frac{1}{2}\nabla_i^2 - \sum_{\alpha}\frac{Z_i}{R_{\alpha i}} + \bar{V}_i\right] = \sum_{i=1}^{N} h_i^{\text{eff}}. \qquad (4)$$

The total energy calculated with the self-consistent field (Hartree–Fock) approximation differs substantially from the true total energy, owing to the neglect of "instantaneous" interactions of the electrons (or collisions): thus for the ethane molecule this difference amounts to 0.8 a.u. or ~ 500 kcal mole^{-1}![18] However, many properties of molecules are reproduced quite well by Hartree–Fock calculation. We first note that bond angles and lengths, angles of rotation, energy differences between rotational isomers, and barriers to internal rotation can be obtained in terms of a model of independent electrons (non-empirical calculations with large basis-sets are envisaged) with an accuracy only slightly inferior to that of the best experiments. We shall therefore regard the self-consistent field approximation as almost the exact Schrödinger equation for the molecule, and use it as a basis for comparing the various semi-empirical methods.

A solution of the Hartree–Fock problem is usually sought in the form of spin orbitals ψ, each of which is written as a product $\psi_i(x_\rho)\sigma_i$, where $\psi_i(x_j) \equiv \psi_i$ is the ith molecular orbital (MO), depending only on the spatial

coordinates x_j of the jth electron, and σ_j is the spin coordinate, assuming the value either $\eta_+(j)$ or $\eta_-(j)$. The molecular orbital ψ_i is presented as a linear combination of atomic orbitals (LCAO) $\varphi\nu \equiv \varphi_\nu(x_j)$:

$$\psi_i = \sum_\nu c_{i\nu}\varphi_\nu. \tag{5}$$

Denoting the ith spin orbital of the jth electron with the spin coordinate $\eta_+(j)$ as

$$\psi_i(j) = (\Sigma_\nu c_{i\nu}\varphi_\nu)\,\eta_+(j),$$

and with the spin coordinate $\eta_-(j)$ as

$$\psi_i(j) = (\Sigma_\nu c_{i\nu}\varphi_\nu)\,\eta_-(j),$$

we write the approximate wave function Ψ for a molecule with a closed electron shell (even number of electrons N) as the antisymmetrised product of the spin orbitals or the Slater determinant

$$\Psi = A\begin{vmatrix} \psi_1(1)\,\psi_1(2) & \dots & \psi_1(N) \\ \bar{\psi}_1(1)\,\bar{\psi}_1(2) & \dots & \bar{\psi}_1(N) \\ \dots & \dots & \dots \\ \psi_{\frac{N}{2}}(1)\,\psi_{\frac{N}{2}}(2) & \dots & \psi_{\frac{N}{2}}(N) \\ \bar{\psi}_{\frac{N}{2}}(1)\,\psi_{\frac{N}{2}}(2) & \dots & \bar{\psi}_{\frac{N}{2}}(N) \end{vmatrix} \equiv A|\psi_1\bar{\psi}_1, \dots, \psi_{\frac{N}{2}}\bar{\psi}_{\frac{N}{2}}| = A\left(1,\bar{1}, \dots, \frac{N}{2}, \frac{\bar{N}}{2}\right), \tag{6}$$

where A is a normalised coefficient determined from the condition

$$\int \Psi\Psi^* d\tau = 0.$$

The variational LCAO-MO method yields Roothaan's equations[19,20], which make it possible to determine the coefficients $c_{i\nu}$, i.e. the fractional involvement of each atomic orbital in the molecular orbitals:

$$\sum_\nu F_{\mu\nu}c_{i\nu} = E_i \sum_\nu S_{\mu\nu}c_{i\nu}. \tag{7}$$

Where the E_i are the orbital energies or eigenvalues of the molecular orbital,

$$S_{\mu\nu} = \int \varphi_\mu^* \varphi_\nu\, d\tau \tag{8}$$

are the overlap integrals, and the

$$F_{\mu\nu} = H_{\mu\nu} + G_{\mu\nu} \tag{9}$$

are the matrix elements of the Fock operator, in which

$$H_{\mu\nu} = \int \varphi_\mu^* \left[-\frac{1}{2}\nabla^2 - \sum V_\alpha(r)\right]\varphi_\nu\, d\tau, \tag{10}$$

$$G_{\mu\nu} = \sum_{\lambda,\sigma} P_{\lambda\sigma}\left[(\mu\nu/\lambda\sigma) - \frac{1}{2}(\mu\sigma/\nu\lambda)\right], \tag{11}$$

$$(\mu\nu/\lambda\sigma) = \int\int \varphi_\mu^*(1)\,\varphi_\nu(1)\,(r_{12})^{-1}\varphi_\lambda^*(2)\,\varphi_\sigma(2)\,d\tau_1\,d\tau_2, \tag{12}$$

$$P_{\lambda\sigma} = 2\sum_i^{\text{occup}} c_{i\lambda}^* c_{i\sigma}, \tag{13}$$

and φ_μ^* is a complex conjugate function with respect to $\varphi\mu$. The $H\mu\nu$ in Eqns. (10)–(13) are matrix elements of the one-electron Hamiltonian, and include both kinetic and potential energy. In conformity with the fundamental idea of the self-consistent field, the potential energy is the energy of the effective electrostatic field $\Sigma V_\alpha(r)$ produced by the nuclei and by the other electrons (the summation extends over all nuclei α). The $G\mu\nu$ are the matrix elements of the effective potential resulting from interelectronic interaction. The dependence of $G_{\mu\nu}$ on the molecular orbitals is determined through the population matrix (the bond-order matrix) $P_{\lambda\sigma}$ in which the summation is made only over occupied molecular orbitals (the factor 2 indicates that each orbital is doubly occupied).

The concept of self-consistency is evident from Eqn. (13): the population matrix depends on the molecular orbitals, whereas Eqn. (7) is intended for determining the coefficients of the molecular orbitals. Self-consistency involves seeking coefficients with which these equations are satisfied. In practice self-consistency is achieved by iteration procedures.

The orbital energies E_i are roots of the secular equation

$$|F_{\mu\nu} - ES_{\mu\nu}| = 0, \tag{14}$$

while the total electronic energy is given by the formula

$$E_{\text{el.}} = \frac{1}{2}\sum_{\mu,\nu} P_{\mu\nu}(H_{\mu\nu} - F_{\mu\nu}). \tag{15}$$

Since (15) is a solution only of the "electronic" Schrödinger equation, the energy of interaction of the nuclei must be added to the energy of the electrons to give the total energy:

$$E = E_{\text{el.}} + \sum_{\alpha>\beta}\sum Z_\alpha Z_\beta / R_{\alpha\beta}. \tag{16}$$

The matrix elements $G\mu\nu$ are usually expressed in terms of Coulombic and exchange operators $K\mu\nu$ and $I\mu\nu$:

$$G_{\mu\nu} = I_{\mu\nu} - K_{\mu\nu}/2, \tag{17}$$

where explicit expressions for $I\mu\nu$ and $K\mu\nu$ can easily be found from Eqns. (11)–(13). Now writing the matrix elements of the kinetic-energy operator $T\mu\nu$ from (10) in the form

$$T_{\mu\nu} = \int \varphi_\mu^* | -\nabla^2/2 | \varphi_\nu\, d\tau, \tag{18}$$

we obtain the matrix form of the Roothaan equations

$$\mathbf{F}c_i = (\mathbf{H} + \mathbf{G})\,\mathbf{c}_i = (\mathbf{T} + \sum_\alpha \mathbf{V}_\alpha + \mathbf{I} - \mathbf{K}/2)\,\mathbf{c}_i = \mathbf{E}_i\mathbf{S}c_i \tag{19}$$

where **F**, **H**, **G**, **T**, $\mathbf{V}_\alpha$, **I**, **K**, and **S** are the matrices whose elements have been discussed above and $\mathbf{c}_i$ is a column of the matrix $c\nu i$.

A few comments on the basis-sets used in quantum-mechanical calculations. The limited (minimal) basal series corresponds to 1s orbitals of hydrogen atoms; 1s, 2s, and 2p (2p_x, 2p_y, 2p_z) orbitals of carbon, nitrogen, and oxygen atoms; etc. Extended basis-sets may involve the use of two or more functions of 1s, 2s, etc. types (i.e. there may be various orbital exponents) and also polarisation functions, e.g. functions of d- and f-types for carbon atoms. It is clear that, the larger the basal series, the better the approximation obtainable to the Hartree–Fock limit.

Semi-empirical calculations usually have a valency basis: in this case the electrons of the inner shells are assigned to the core, and are assumed to introduce a correction to the electrostatic field produced by the nucleus. In π-electron theories it is assumed, moreover, that all σ-electrons belong to the core, and only the properties of the π-electron system are examined.

Thus the first and most important "simplification" in the Roothaan equations is the general use of the valency approximation in semi-empirical theories. With regard to the resulting change in structure of the equations it is obvious that formula (10) for the effective Hamiltonian $H\mu\nu$ can then be rewritten

$$H_{\mu\nu} = \int \varphi_\mu^* \left[-\frac{1}{2}\nabla^2 - \sum_A V_A(r)\right]\varphi_\nu\, d\tau, \tag{20}$$

where the operator in the integrand is the effective potential energy of the electrostatic field due to the atomic cores $V_A(r)$ summed over all atoms A belonging to the molecule (the core of the atom is taken to be its nucleus together with the electrons of its inner shells). It therefore makes sense to replace the nuclear charges Z_α and Z_β by the core charges Z'_A and Z'_B, so that Eqn. (16) will become

$$E = E_{el.} + \sum_{A>B}\sum Z'_A Z'_B / R_{AB} . \qquad (16a)$$

In most semi-empirical methods functions of the Slater type

$$\varphi(r, \theta, \varphi) = R_{nl}(r) Y_{lm}(\theta, \varphi), \qquad (21)$$

(where n, l, m are quantum numbers (principal, azimuthal, magnetic) and r, θ, φ are the spherical coordinates of the electron) are used as atomic orbitals. For the radial part R_{nl} with $n \leq 3$ we have

$$R_{nl}(r) = (2\zeta)^{n+1/2} [(2n)!]^{-1/2} r^{n-1} \exp(-\zeta r), \qquad (22)$$

where ζ is the orbital exponent. The spherical functions $Y_{lm}(\theta, \varphi)$ characterising the angular distribution, however, are expressed in terms of Legendre polynomials. In conformity with Slater's view, the orbital exponentials are written

$$\zeta = (Z - s)/n^*, \qquad (23)$$

where Z is the nuclear charge, s the shielding constant, and n^* the effective principal quantum number. Values of s and n^* for the orbitals used in quantum-mechanical calculations of molecules have been tabulated and are given in several monographs[21-23].

Further "simplifications" of the Roothaan equations involve neglecting some integrals in Eqns. (10) and (11) and parametrising several other integrals. There would be no need for this, but for the great bulk of calculations caused by a total number of integrals of the order of N^4 (where N is the number of basal orbitals), as is readily seen from formula (11). In the evaluation of the equilibrium geometry corresponding to an absolute energy minimum or of barriers to internal rotation, however, energy calculations should be repeated several and sometimes many times (it is necessary to vary the geometric parameters). By neglecting certain integrals, semi-empirical methods enable the time, required to calculate on a computer (BESM-6 type) the "total" energy of a molecule with a fixed geometry, to be reduced to a few minutes, and then it really becomes possible to investigate various conformations for a large set of molecules.

The evolution of quantum chemistry can be regarded as a gradual transition from simple to more complicated methods, taking into account a larger number of integrals: with the years an increasingly distinct tendency has developed to obtain the best possible approximation to the Hartree–Fock limit even for organic molecules of "average" dimensions. The non-empirical calculations of the electronic structure of the pyrrole, pyridine, and pyrazine molecules made by Clementi and Davis[24,25] may be cited as example.

Ten to fifteen years ago, of course, such calculations were technically impracticable, and the Roothaan equations were applied only to diatomic molecules. The electronic structure of large unsaturated organic molecules was usually investigated by the simple Hückel method[26,27] on the hypothesis of σ–π separation. More complicated π-electron schemes then acquired popularity, in particular the Pariser–Parr–Pople (PPP) method[28,29], which took into account a rather larger number of integrals, but as before included the σ-electrons in the core. The next considerable advance was to include the σ-electrons in the scheme of calculation by means of the extended Hückel method[30]. Finally, methods appeared using the valency approximation and involving partial or complete neglect of differential overlap[22,31-34]. Since, with a sufficiently large basis-set, non-empirical calculations by Roothaan's method give reliable predictions of geometric parameters and barriers to internal rotation, as has been mentioned, it is not surprising that the improvement of semi-empirical theories has been accompanied by an increasing rôle in calculations of the geometry of polyatomic molecules.

Methods based on localised orbitals, and originating in the "old-fashioned" valence-bond method[35], were developed in parallel with LCAO-MO methods. As early as the beginning of the 1950s Lennard-Jones and Hall[36-38] showed that unitary transformations of molecular orbitals preserve the Slater determinant and enable localised to be expressed in terms of delocalised molecular orbitals (the molecular wave function remaining unchanged). Ideas developed by the above workers and independently by Fock[39] gave rise to the theory of separated electron pairs[40-43], in which the wave function is represented by an antisymmetrised product of two-electron functions (biorbitals or geminals). Although equations similar in meaning to the Roothaan equations could be obtained for such functions, for a long time no appreciable progress was made in specific calculations. Only comparatively recently have methods based on localised orbitals become widely used both in non-empirical and in semi-empirical calculations.

The following Sections will examine semi-empirical methods in order of increasing complexity. The simplest methods (of the Hückel type) make no explicit allowance for interaction between electrons, and utilise only a few of the most important integrals. Since, however, these integrals are too remote in meaning from those in the Roothaan equations, they must be parametrised by means of experimental data (the parameters are mostly found from a comparison of calculated and experimental properties of simple molecules). More complicated methods, in which interelectronic interaction is explicit (methods involving complete or partial neglect of differential overlap), require the evaluation of a considerably larger number of integrals together with a self-consistency procedure. Finally, the last Section will examine calculations with localised molecular orbitals, which in principle are already beyond the scope of the Hartree–Fock approximation. The aim is not to investigate in which cases and for which molecular characteristics a particular method should be employed: the more modest aim is pursued of discussing the results obtained by various methods for the geometry of molecules and conformational energies, and of giving a comparative assessment of the reliability and the accuracy of these methods.

III. SIMPLE HÜCKEL METHOD

The simple Hückel method is used in the π-electron approximation to investigate the electronic structure of unsaturated systems. The idea behind this method is extremely simple. If a self-consistency procedure is applied to the Hartree–Fock equations for π-electrons, the molecular orbitals will be solutions of Eqn. (9), in which the matrix elements $F_{\mu\nu}$ can be regarded as constants:

$$F_{\mu\mu} = \alpha_\mu; \; F_{\mu\nu} = \beta_{\mu\nu} \qquad (24)$$

where $\alpha\mu$ is termed a Coulombic integral, and $\beta\mu\nu$ a resonance integral.

In the Hückel method $\alpha\mu$ and $\beta\mu\nu$ are usually regarded as empirical parameters. It is assumed furthermore that the matrix of the overlap integrals is identical with the unit matrix, while the resonance integrals, corresponding to non-bonded atoms, are assumed to be zero. Since no explicit allowance for interelectronic interaction is made in the Hückel method, there is no need for a complicated self-consistency procedure. Solving the problem now reduces to finding the roots of the secular equation (14) and determining the coefficients of the molecular orbitals.

Without considering the further simplifications introduced for π-electron systems or methods of estimating the parameters $\alpha\mu$ and $\beta\mu\nu$, we merely note that this method is unsuitable for completely calculating the geometry of a molecule. In several cases, however, empirical relations between bond length and bond order, which were especially popular fifteen years ago, can be used to assess e.g. carbon–carbon bond lengths in fused aromatic systems such as naphthalene, phenanthrene, etc.

Table 1. Dependence of resonance integral (25) on internuclear distance.

Å	k^{14}	k^{15}	Å	k^{14}	k^{15}
1.20	1.71	1.38	1.45	0.83	0.91
1.33	1.23	1.11	1.54	0.57	0.78
1.397	1.00	1.00			

The Hückel method is usually applied to molecules having a planar conjugated system. If the length of a bond which transmits the conjugation (e.g. the central carbon–carbon bond in biphenyl) is changed by the repulsion of non-bonded atoms, the resonance integral is represented by the formula

$$\beta = k\beta_0, \qquad (25)$$

where β_0 is the "standard" value of the resonance integral and k is a constant, whose variation with the carbon–carbon bond length is given in Table 1. If, however, the repulsion of non-bonded atoms leads to a loss of coplanarity, a correction is made to the resonance integral of the bond relative to which the parts of the molecule are rotated. The resonance integral is then regarded as a function of the angle of rotation φ (e.g. between the planes of the phenyl rings in biphenyl) and is calculated by means of the formulae

$$\beta_\varphi = \beta_{\varphi=0}\cos\varphi \qquad (26)$$

and

$$\beta_\varphi = \beta_{\varphi=0}\cos^2\varphi\,. \qquad (27)$$

These equations are based on the proportionality noted by Mulliken[41–46] between resonance and overlap integrals; probably their first applications were reported in Refs. 47 and 48.

Neither in accuracy nor in relative validity do expressions of such type differ from the empirical formulae used in classical calculations[49,50], where the analogue of the resonance integral is the empirical constant U_0. Nor can attempts to obtain more complicated formulae for the resonance integral by the simple Hückel method be regarded as sufficiently soundly based. This applies in particular to the suggested[51] relation

$$\beta = \beta_0 \frac{S/(1+S)}{S_0/(1+S_0)}, \qquad (28)$$

which follows from Mulliken's "magic" formula[46] (S and S_0 are overlap integrals).

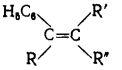
Adrian[52] computed the equilibrium conformations of the triphenylmethyl radical (I), biphenyl (II), *cis*-stilbene (III), *cis*-azobenzene (IV), and the *pp'*-dimethoxyphenylnitric oxide radical (V). Resonance integrals for the carbon–carbon bonds about which rotation occurs were estimated by Wheland's method[53], which gave relations between β and φ closely similar to (27). Repulsions of non-bonded atoms compete with conjugation in these molecules (I)–(V). The H...H interactions were allowed for by means of Hirschfelder and Linnett's potential curve[54], and the C...H interactions by means of the relation $f_{C...H} = 2.3 f_{H...H}$ (interactions between carbon atoms were disregarded). The calculated angles φ of rotation of the phenyl rings for the five compounds (I)–(V) were respectively 32°, 20–30°, 30–40°, > 40°, and ~ 25°, agreeing quite well with the experimental values.

Goodwin and Morton-Blake[55] tried to solve the "converse" problem–to obtain the parameters of the H...H potential from data on the equilibrium conformation of biphenyl in the vapour (the angle between the phenyl rings is $\varphi = 42°$) and the approximate expression for the conjugation energy[56]

$$\varepsilon_\pi = 0.196\beta^* \cos^2\varphi$$

with respect to a system of two isolated benzene rings. They adopted the value $\beta^* = -32.5$ kcal mole^{-1}. The calculated H...H potential (it has no minimum, of course, since only repulsion was considered) was rather "more rigid" than other published potentials. This is due partly to the neglect of C...C and C...H interactions.

Favini and Simonetta[57] examined the conformations of the phenylated and methylated ethylenes



(R, R', and R'' are hydrogen atoms or phenyl and methyl groups). The ideal bond angles in ethylene and its derivatives were assumed to be 120°, corresponding to sp^2 hybridisation of the carbon atoms. The C–R, C–R', etc. bond lengths were computed by an iteration procedure involving calculating bond orders in the Hückel approximation for some standard geometry, and determining the bond lengths by means of Coulson's dependence[58] of bond length on bond order. Resonance integrals β were then calculated for the resulting geometry, bond orders and lengths were redetermined, and the procedure repeated until changes in bond lengths became less than 0.005 Å. Rotations of the phenyl rings relative to the plane of the ethylene system were allowed for by means of formula (26). Finally, the energy of interaction of non-bonded atoms was calculated by means of Kitaigorodskii potentials[59].

The most interesting calculated results are the angles of rotation of the phenyl rings relative to the plane of the ethylenic system (the distortions of the bond angles lay within the limits of accuracy of the calculation). Twenty compounds of this type gave angles of rotation of 17–60°.

Another paper by Italian authors [60] gave a similar calculation of the equilibrium conformation of the *trans*-$\alpha\beta$-dicyanostilbene molecule. Unfortunately, reliable structural data are as yet lacking for the large majority of these compounds.

The problem of rotation about bonds that transmit conjugation has been investigated not only by the simple Hückel method. Dewar and Harget [61] proposed a method of evaluating resonance integrals from thermochemical data and used Bartell potentials [62] to obtain a dihedral angle of $\varphi = 40°$ in biphenyl, in excellent agreement with experiment (42°). [63] Skancke [64] worked out the parametrisation of the zero differential overlap method for π-electrons (actually for the PPP method), which enabled the conformations of various fluorinated biphenyls to be predicted with good accuracy [65]. In this series of compounds the dihedral angle between the phenyl rings is increased by the entry of substituents at positions 2 and 6, reaching a maximum of 70° in decafluorobiphenyl [66]. This tendency is apparent also in calculations taking into account non-bonded interactions and the π-electron energy. A similar approach, but with use of the CNDO valency approximation (Section V), was made by Sekigawa [67] to investigating the conformations of nitronaphthalenes and certain other compounds of this type. The results of his calculations are almost identical with those obtained for the same compounds by means of the mechanical model of the molecule [49].

In the above examples empirical model methods are ultimately used, since the search for equilibrium conformations is based on the examination of non-bonded interactions. Only conjugation energies, bond orders, and certain other quantities are estimated by semi-empirical methods of quantum chemistry. The term "quantum-mechanical" should properly be applied only to calculations that give the total energy of the molecule. As already mentioned, the optimal conformers would then correspond to minima of the total energy; the heat of isomerisation is given by the difference between the total energies of the isomers; etc. Henceforward we shall consider parametric methods enabling the total energy of the molecule to be estimated.

IV. EXTENDED HÜCKEL METHOD

The extended Hückel method (EHM) uses the valency approximation and the assumption that the matrix elements of the Fock operator $F_{\mu\nu}$ are independent of the coefficients of the molecular orbitals:

$$F_{\mu\nu} = H_{\mu\nu}^{\text{eff}}. \qquad (29)$$

Comparison of Eqn. (29) with (9)–(13) shows firstly that the extended method does not allow explicitly for the interaction of the electrons (11) and secondly that the effective one-electron Hamiltonian takes account both of the kinetic energy of the electrons and of the effect on them of the electrostatic field of the core, but makes no separation of these two completely different kinds of effect. In contrast to the simple Hückel method (24), however, the extended method covers all non-diagonal elements of the one-electron Hamiltonian. This is very important in conformational analysis: it is because the non-diagonal elements differ in different conformations of such molecules as e.g. n-butane that these conformations have different energies. Another virtue of the extended Hückel method is that it takes into account all the valency electrons of the molecule, whereas methods used until the 1960s usually covered only the π-electrons, the σ-electrons being confined to the core.

Hoffmann [68], having demonstrated the great predictive power of this method, suggested using the ionisation potentials of the corresponding valency states of the atoms as the diagonal matrix elements $H_{\mu\mu}$. For hydrocarbon molecules, in particular, he used the values (in kcal mole^{-1}) $H_{\mu\mu}(1s\text{H}) = -313.6$, $H_{\mu\mu}(2s\text{C}) = -493.5$, and $H_{\mu\mu}(2p\text{C}) = -262.9$. [69,70] The non-diagonal matrix elements $H_{\mu\nu}$ are usually obtained by means of the Wolfsberg–Helmholtz relation [71]

$$H_{\mu\nu} = 0.5K(H_{\mu\mu} + H_{\nu\nu}) \cdot S_{\mu\nu}, \qquad (30)$$

where K is an empirical constant and the $S_{\mu\nu}$ are the overlap integrals of the Slater orbitals.

Choosing the value of K is the most difficult part of the whole scheme of calculation [72]. If Mulliken's approximation is adopted [46], K should be unity. But calculations for homonuclear diatomic molecules then give absurd results. It is therefore usually assumed that $K > 1$, and in Hoffmann's work and several other calculations of conformations and conformational energies the value of K is taken to be 1.75.

The non-diagonal elements $H_{\mu\nu}$ are not only estimated by means of formula (30), in which the arithmetic mean of the diagonal elements $H_{\mu\mu}$ and $H_{\nu\nu}$ is used, but sometimes from the geometric mean of these quantities [73,74]:

$$H_{\mu\nu} = K\sqrt{H_{\mu\mu}H_{\nu\nu}} \cdot S_{\mu\nu}. \qquad (31)$$

Formula (31) can be regarded as just as valid as (30). The proportionality coefficient K should exceed unity in this case, and the best agreement with experiment is obtained when $K = 1.75$.

An interesting attempt was made to avoid altogether the empirical constant K, and write the non-diagonal matrix elements of the Hamiltonian in the form [75]

$$H_{\mu\nu} = (2 - |S_{\mu\nu}|)S_{\mu\nu}(H_{\mu\mu} + H_{\nu\nu})/2. \qquad (32)$$

Calculations in the extended Hückel method are quite simple: they merely involve evaluating the overlap integrals $S_{\mu\nu}$, setting up the matrix H, and solving the set of equations

$$\sum_{\mu=1}^{n} [H_{\mu\nu} - ES_{\mu\nu}]c_{\mu} = 0, \quad \nu = 1, 2, \ldots, n, \qquad (33)$$

where n is the number of atomic orbitals. Allowing for the double occupation of each level, we take the "total" energy to be given by the sum of the orbital energies E_i of the occupied molecular orbitals:

$$E_{\text{total}} = 2\sum_{i} E_i.$$

The computer time necessary to estimate the coefficients $c_{\mu\nu}$ and compute the "total" energy is of the same order as the time required to calculate empirical potential functions. Thus only 10 s is required to calculate ethane [68]. Within the framework of the extended Hückel method, therefore, it is possible to seek the minimum total energy and calculate energy differences between rotational isomers and barriers to internal rotation.

We return to Hoffmann's parametrisation [68], and examine the results obtained in the calculation of conformations. The three conformations of propane—(I) with both methyl groups in the staggered position with respect to the methylene group, (II) with one methyl in the staggered position and the other in the eclipsed position, and (III) with both methyls in the eclipsed position—have calculated energies of −8022.32, −8016.69, and −8009.91

kcal mole^{-1}, whence it follows that (I) is the most stable form. But the calculated difference in energy between (I) and (II) is 5.63 kcal mole^{-1}, which considerably exceeds the experimental value[76]. The most favourable of the twelve conformations of n-butane is the *trans*(or *anti*)-form with the carbon–hydrogen bonds in the staggered position, which is consistent with electron-diffraction data[77]. However, the barrier to internal rotation (the difference in energy between *cis*- and *trans*-forms) is too large in comparison with the experimental value[78] (27 and 6.92 kcal mole^{-1}). The calculated barrier to internal rotation in ethane is also overestimated: 4.0 in comparison with the experimental value[79] of 2.93 kcal mole^{-1}. Calculated energies of isomerisation are also rather too high: thus for the isomerisation of n-butane into isobutane calculation gives 2.3 kcal mole^{-1}, whereas the experimental value[80] is 1.6 kcal mole^{-1}.

Calculation of the conformations of cycloalkanes has yielded interesting results. Like most empirical theories, the extended Hückel method gives for cyclobutane a minimum corresponding to the planar form. In cyclopentane the planar form is unfavoured, but the half-chair (C_2) is more favoured than the "envelope" (C_S) by 1.8 kcal mole^{-1}. This result agrees neither with empirical estimates nor with electron-diffraction data[81] proving the equivalence of these forms and the absence of hindrance to pseudorotation. The calculated difference in energy between chair and boat conformations of cyclohexane (17.7 kcal mole^{-1}) is about double the experimental value.

Hoffmann's paper was the first of a stream of predictions of the geometry and the conformational energies of molecules, and many workers regarded it as a triumph of quantum chemistry. Other authors, on the other hand, considered that the accuracy of the predictions obtained by the extended method was too poor; in any case, it is substantially inferior to that of model methods using atom–atom potentials. Subsequent Hartree–Fock calculations of the conformations of simple molecules helped to establish a moderate attitude: the extended Hückel method is useful for rough conformational calculations, but gives inaccurate values of conformational energies, and in some cases an incorrect assignment of favoured conformers.

The above examples show that the extended Hückel method in Hoffmann's parametrisation leads to a re-evaluation of the part played by the steric factor. Hoffmann calculated conformational energies for experimental bond lengths and valency angles. Strictly speaking, a minimum total energy should be sought with respect to all internal parameters, including bonds and angles. Unfortunately such a procedure does not lead to agreement with experiment: Table 2 shows that the calculated geometric parameters are far removed from the experimental values†. Conformational energies obtained with the optimised geometry are too low. Thus in Hoffmann's method optimisation of the geometry does not give agreement with experiment. Nor could better agreement be obtained by changing the parametrisation. Thus if the value 1.2 instead of 1.0 is adopted for the Slater exponent 1*s*H, calculation will give the correct barrier in ethane, but strong divergence from experiment for the difference in energy between chair and boat conformations of cyclohexane.

† The reason why the extended method may give reasonable conformational energies, while being completely unsuitable for predicting the geometry of molecules, will be indicated in Section V.

The formalism of the extended Hückel method has been compared[74,83,84] with Roothaan's formalism, and the main sources of error in the extended method have been indicated. According to Allen[74,84] a considerable proportion of the error is due to change in the electrostatic potential $\Sigma_A V_A(r)$ in Eqn. (20) during deformations of bond angles and rotations about bonds. Therefore, whereas the extended method works satisfactorily for hydrocarbons, it often predicts, for molecules whose atoms bear large excess charges, a geometry that is markedly different from the experimental geometry. Thus for the water molecule the extended method yields an HOH equilibrium angle of 140°, whereas the experimental angle is 104.5°. For the same reason the shape of the potential curve for internal rotation in the hydrogen peroxide molecule is opposite to the experimental curve.

Table 2. Geometric parameters corresponding to minimum energy in the extended Hückel method[68,82].

Molecule	Bond	Bond length, Å		Valency angle	Value of angle	
		calc.	expt.		calc.	expt.
CH_4	C—H	1.02	1.09			
$H_3C—CH_3$	C—C	1.92	1.53			
	C—H	1.00	1.10			
$H_2C=CH_2$	C=C	1.47	1.33	HCH	125°	
	C—H	0.95	1.08			
	C=C	1.52	1.33	HCH	120.7°	115.6°
	C—H	0.92	1.08			

A numerical investigation of the dependence of the non-diagonal matrix elements of the one-electron Hamiltonian on the distance between the atoms showed[83] that the proportionality of $H_{\mu\nu}$ and $S_{\mu\nu}$ expressed by Eqn. (30) is satisfied fairly accurately only if the atomic orbitals φ_μ and φ_ν are not immediate neighbours (it is probably for this reason that the extended method is suitable for conformational calculations). However, neighbouring atoms show large departures from proportionality, caused by the kinetic portion $(\varphi_\mu | -\frac{1}{2}\nabla^2 | \varphi_\nu)$ of the Hamiltonian in Eqn. (10). This non-proportionality is primarily responsible for the constant K differing from unity in the Wolfsberg–Helmholtz relation.

In spite of the obvious defects of the extended Hückel method, it is widely used for theoretical investigations of the conformations of structurally similar molecules. Van Eijck[85], who calculated the conformations of numerous carboxylic acids, concluded that the method predicts the correct equilibrium structure for these compounds in nearly every case: only the calculated barriers to internal rotation showed poor agreement with experiment. Pachler and Tollenaere[86] calculated conformational energies for substituted ethanes—fluoroethane, 1,2-difluoroethane, ethanol, propionitrile, ethylene glycol, 2-fluoroethanol, and succinonitrile—and obtained good agreement between calculated and experimental barriers to rotation by using experimental bond lengths and angles and adopting the value 1.2 for the Slater exponent 1*s*H (with exponent of 1.0 the resulting barriers were overestimated by 30–80%). In full agreement with experiment, calculation predicts preference for the gauche forms of 1,2-difluoroethane, ethylene glycol, 2-fluoroethanol, and succinonitrile. However, the calculated energy differences between the gauche and *trans*-forms are too large in comparison with the experimental differences.

Because of the simplicity of programming and the small consumption of computer time, the extended Hückel method rapidly gained popularity with biochemists investigating the conformational states of complicated bio-organic molecules. Thus conformational maps have been calculated[87] for dipeptides, the structural units of protein molecules; the conformations of amino-acids have been investigated[88]; and Long and Goldstein have predicted[89] the conformations of nicotinamide and related amides. Finally, mention may be made of work done by Kier[90], who calculated the molecular conformations of many medicinals, and claimed the start of a new line of scientific advance—quantum pharmacology.

Pullman[91-93] used the extended method to investigate the conformations of nucleosides, photodimers of thymine, and several other molecules related to components of nucleic acids. He was interested not only in the problems of finding the preferred conformers but also in the charge distribution on the atoms. The calculated charges on the atoms in nucleosides were numerically too large: although no experimental methods are available for determining charge, it is improbable that the excess charge on the oxygen atoms in β-D-ribose and in nitrogen bases would reach the calculated 1.5 electron.

An iteration procedure of the extended Hückel method (IEHM) was suggested[94,95] to obtain more realistic values of the charges and refine the conformational energies. Without going into details of the application of this procedure, we note that it yields reasonable charges on the atoms, and in some cases more reliable conformational energies. However, since the time required to calculate the total energy is appreciably increased, while the significance of the Hamiltonian is not essentially changed, the value of the procedure in conformational calculations is not very great.

V. METHODS OF ZERO DIFFERENTIAL OVERLAP

Pople[31-33] and Dewar[97,98] worked out several semi-empirical self-consistent field methods in the valency approximation. These were close in physical meaning to the Hartree–Fock LCAO-MO procedure, but were considerably simpler and accessible to many chemists having an electronic computer at their disposal.

The most laborious stage in solving Roothaan's equations consists in evaluating the two-electron integrals (11) and (12). Semi-empirical schemes have been constructed with the idea of partly or completely avoiding this complicated procedure. But simply neglecting these integrals strongly distorts the structure of Roothaan's equations: the molecular orbitals ψ_i and the orbital energies E_i become non-invariant with respect to (i) transformations of the coordinates—translation and rotation of the axes—and (ii) change in hybridisation: in particular, replacement of the $2s$, $2p_x$, $2p_y$, and $2p_z$ orbitals of the carbon atom by hybrid sp^3 orbitals will give different solutions of the equations. Although breakdown of hybridisational invariance may still be accepted in several cases, by arranging to use molecular orbitals of a certain type (this procedure is used in calculations by the extended Hückel method), loss of invariance of type (i) is simply intolerable. Indeed, any author is free to choose a system of coordinates in the molecule as he thinks fit, and non-invariance with respect to transformations of the coordinate axes makes it impossible to compare results obtained by different workers. The idea underlying methods of zero differential overlap (ZDO) is the partial or complete neglect of products of atomic orbitals of the type $\varphi_\mu\varphi_\nu$ ($\mu \neq \nu$) and the choice of approximations that leave the Roothaan equations invariant with respect both to orthogonal transformations of the basis and to change in hybridisation.

The method of complete neglect of differential overlap (CNDO)[31,32] involves neglect of integrals of the type (Eqn. 12)

$$(\mu\nu/\lambda\sigma) = 0 \text{ with } \mu \neq \nu,\ \lambda \neq \sigma \tag{34}$$

but it is assumed that

$$\gamma_{\lambda\mu} = (\lambda\lambda\,|\,\mu\mu) \neq 0. \tag{35}$$

This disrupts the invariance of the Roothaan equations, and only further approximations will restore it. It is assumed firstly that $\gamma_{\mu\nu}$ depends solely on the type of atoms to which the orbitals φ_μ and φ_ν belong, not on the type of orbital. Thus γ_{AB} is a measure of the mean repulsion of electrons in valency orbitals of the atom A and the atom B. Combining this postulate with formulae (34) and (35), we obtain instead of (9)–(13) the equations

$$F_{\mu\mu} = H_{\mu\mu} - \frac{1}{2}P_{\mu\mu}\gamma_{AA} + \sum_{B(\neq A)} P_{BB}\gamma_{AB}, \tag{36}$$

$$F_{\mu\nu} = H_{\mu\nu} - \frac{1}{2}P_{\mu\nu}\gamma_{\mu\nu}, \tag{37}$$

$$P_{BB} = \sum_{\nu}^{B} P_{\nu\nu}, \tag{38}$$

$$H_{\mu\mu} = \left(\mu\left|-\frac{1}{2}\Delta^2 - V_A\right|\mu\right) - \sum_{B(\neq A)}(\mu\,|\,V_B\,|\,\mu) = U_{\mu\mu} - \sum_{B(\neq A)} V_{AB}, \tag{39}$$

where the subscripts μ refer to the atom A ($\mu \equiv \varphi_\mu$), P_{BB} in (38) is the aggregate electron density of valency electrons on atom B, and $U_{\mu\mu}$ is the energy of the atomic orbital φ_μ regarded as an empirical parameter. Equations (36)–(39) restore the invariance with respect to orthogonal transformations. A further simplification has been introduced into Eqn. (39): the matrix elements $(\mu\,|\,V_B\,|\,\nu)$, where φ_μ and φ_ν belong to the same atom A, are zero if $\mu \neq \nu$; if, however, $\mu = \nu$, we have $(\mu\,|\,V_B\,|\,\mu) = V_{AB}$.

The non-diagonal matrix elements $H_{\mu\nu}$ in (37) are found empirically on the assumption that they are proportional to the overlap integrals $S_{\mu\nu}$:

$$H_{\mu\nu} = \beta_{\mu\nu} = \beta^0_{AB}S_{\mu\nu}, \tag{40}$$

where β^0_{AB} is an empirical parameter depending on the nature of the atoms A and B. Increments β^0_A and β^0_B are adopted for each atom, and β^0_{AB} is then computed as the arithmetic mean of these increments:

$$\beta^0_{AB} = (\beta^0_A + \beta^0_B)/2. \tag{41}$$

The proportional relation (40), in contrast to the Wolfsberg–Helmholtz formula (30), does not disrupt the invariance of the equations with respect to transformations of the basis-set. Bearing in mind that φ_μ refers to atom A, and φ_ν to B, we find from (40) for the non-diagonal elements of the Fock matrix the expression

$$F_{\mu\nu} = \beta^0_{AB}S_{\mu\nu} - \frac{1}{2}P_{\mu\nu}\gamma_{AB}. \tag{42}$$

An expression for the total energy in the CNDO/1 approximation[31] can now be readily obtained:

$$E_{\text{total}} = \sum_A E_A + \sum_{A>B}\sum E_{AB}, \tag{43}$$

where

$$E_A = \sum_{\mu}^{A} P_{\mu\mu}U_{\mu\mu} + \frac{1}{2}\sum_{\mu}^{A}\sum_{\nu}^{A}\left(P_{\mu\mu}P_{\nu\nu} - \frac{1}{2}P^2_{\mu\nu}\right)\gamma_{AA} \tag{44}$$

and

$$E_{AB} = \sum_{\mu}^{A}\sum_{\nu}^{B}\left(2P_{\mu\nu}\beta_{\mu\nu} - \frac{1}{2}P_{\mu\nu}^2\gamma_{AB}\right) + \\ + (Z'_A Z'_B R_{AB}^{-1} - P_{AA}V_{AB} - P_{BB}V_{BA} + P_{AA}P_{AB}V_{AB}). \quad (45)$$

The energies of the atomic orbitals $U_{\mu\mu}$ are expressed in this approximation in terms of mean ionisation potentials I_μ:

$$U_{\mu\mu} = -I_\mu - (Z-1)\gamma_{AA}. \quad (46)$$

Calculations by the CNDO/1 method give bond lengths in diatomic molecules that are too short and bond energies that are too large. Polyatomic molecules, however, are, roughly speaking, "too compressed". Pople and Segal[32] therefore proposed a different parametrisation (CNDO/2), which subsequently became widely accepted. Firstly it is assumed that

$$V_{AB} = Z'_B\gamma_{AB}. \quad (47)$$

Application of this relation enables "the effect of 'penetration' of one atom into the electron shell of the other to be diminished" (however, the physical justification for this is weak). Further, the parameter $U_{\mu\mu}$ is estimated by averaging the ionisation potential I_μ and the electron affinity A_μ:

$$U_{\mu\mu} = -\frac{1}{2}(I_\mu + A_\mu) + \left(Z' - \frac{1}{2}\right)\gamma_{AA}. \quad (48)$$

For the matrix elements of the Fock operator we then obtain the formulae

$$F_{\mu\mu} = -\frac{1}{2}(I_\mu + A_\mu) + \left[(P_{AA} - Z'_A) - \frac{1}{2}(P_{\mu\mu} - 1)\right]\gamma_{AB} + \sum_{B(\neq A)}(P_{BB} - Z'_B)\gamma_{AB} \quad (49)$$

$$F_{\mu\nu} = \beta^0_{AB}S_{\mu\nu} - \frac{1}{2}P_{\mu\nu}\gamma_{AB}. \quad (50)$$

The Slater basis-set with exponents 1 and 2 for the hydrogen atoms is used in computing the overlap integrals $S\mu\nu$. In contrast to the extended Hückel method, complete neglect of differential overlap requires self-consistency procedures. The iteration procedure consists in making initial estimates of the coefficients of the linear combination of orbitals from theories of Hückel type

$$F^{(0)}_{\mu\mu} = -\frac{1}{2}(I_\mu + A_\mu), \quad (51)$$

$$F^{(0)}_{\mu\nu} = \beta^0_{AB}S_{\mu\nu}, \quad (52)$$

and computing the total energy and the matrix elements $F\mu\nu$ until self-consistency is attained.

The success of the CNDO/2 method depends substantially on the parametrisation, especially on the choice of proportionality constants β^0_{AB} in Eqn. (40) (more precisely on the choice of the atomic constants $\beta^0_A, \beta^0_B, \ldots$). Pople and Segal[32] selected these constants to give the best possible reproduction of the results of non-empirical calculations of corresponding diatomic molecules made with the same set of atomic orbitals. Use of their parametrisation yields reasonable geometric parameters, conformational energies, and barriers to internal rotation. In any case, it becomes possible to make a serious search for a minimum total energy in order to obtain the geometry of the molecule and the energy characteristics of the conformers: in the extended Hückel method such a search leads in many cases to absurd results.

Table 3, based on Gordon's results[99], gives an idea of the extent of agreement between calculated and experimental values (bond lengths are given only to hundredths of an Ångström unit; extremal values reached during rotation are given for the calculated valency angles; and references to the experiments will be found in the original paper). Bond lengths are seen to be predicted with a mean accuracy of 0.1 Å, and valency angles to a few degrees. Nevertheless, the divergence between calculation and experiment is in some cases too large—e.g. the oxygen–oxygen bond length and the HOO valency angle in the hydrogen peroxide molecule, and the oxygen–fluorine bond length in the F_2O_2 molecule.

Table 3. Molecular geometry predicted by CNDO/2 method with Pople–Segal parameters.

Molecule	Bond	Bond length, Å		Valency angle	Angle, degrees	
		calc.	expt.		calc.	expt.
H_3C-CH_3	C—C	1.46	1.52	HCH	106.0—106.5	107.8
	C—H	1.12	1.10			
H_3C-NH_2	C—N	1.41	1.47	CNH	108.7—107.5	112.3
	C—H	1.12	1.09	HNH	103.8—104.2	105.8
	N—H	1.07	1.01			
H_3COH	C—C	1.37	1.43	HCO	110.9—110.7	109.5
	C—H	1.12	1.09	HCH	108.0—108.2	109.5
	O—H	1.03	0.94	COH	106.6—105.0	109.5
HO—OH	O—O	1.22	1.47	OOH	110.8—105.0	94.8
	O—H	1.04	0.95			
FO—FO	O—O	1.22	1.22	OOF	109.0—105.6	109.5
	O—F	1.18	1.57			
H_2N-H_2N	N—N	1.34	1.45		106.5—110.6	112.0
	N—H	1.07	1.20	HNH	102.5—103.0	105.8

Table 4. Barriers to internal rotation calculated by CNDO/2 method.

Molecule	Height of barrier, kcal mole^{-1}		Molecule	Height of barrier, kcal mole^{-1}	
	calc.	expt.		calc.	expt.
cis-H_2O_2	5.16 [99]	7.0	CH_3-CH_2F	2.00 [99]	3.30
trans-H_2O_2	0 [99]	1.1			
CH_3OH	0.78 [99]	1.07	CH_3-CHF_2	1.88 [99]	3.18
	0.67 [32]				
CH_3NH_2	1.57 [99]	1.97	CH_3-CF_3	1.76 [99]	3.48
	1.21 [32]				
C_2H_6	2.18 [99]	2.93	CF_3-CHF	1.46 [99]	4.58
	2.32 [32]				
C_3H_8	2.20 [101]	3.6	$CF-CHF_2$	1.22 [99]	3.51
iso-C_4H_{10}	2.64 [101]	3.9	$CF-CF_3$	1.07 [99]	3.92
C_3H_6	1.16 [102]	1.98	*trans*-FCH:$CHCH_3$	1.30 [99]	2.20
	1.00 [101]				
cis-2-C_4H_8	0.44 [101]	0.75	*cis*-FCH:$CHCH_3$	0.93 [99]	1.06
CH_3CHO	0.71 [103]	1.16	CH_2:$CFCH_3$	0.88 [99]	2.43
HCOOH	34.9 [103]	17.0	CF_2:$CHCH_3$	0.96 [99]	1.25

Table 4, compiled from results in several papers (references to the experimental work will be found in a review[100]), gives calculated barriers to internal rotation. Comparison of the values calculated for methanol, methylamine, and ethane shows that the two variants of the method—CNDO/1 and CNDO/2—give closely similar results. It is evident that this method almost always underestimates the barriers, as a consequence of partial neglect of two-electron integrals and/or the parametrisation. Despite the discrepancy between calculated and

experimental values, however, the trend in the variation of the barriers is in the main correctly reproduced. Thus the proportions 3 : 2 : 1 for ethane, methylamine, and methanol are quite well satisfied[100], and the assignment of minima and maxima of the total energy during internal rotation is correct in all cases other than for hydrogen peroxide. With fluorinated derivatives calculation gives the right assignment of stable forms, but poor agreement with experiment both in the numerical values of the barriers and in the trend of their variation on passing from one molecule to another.

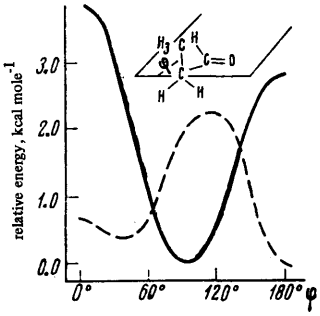


Figure 1. Variation in energy of propionaldehyde molecule during rotation of the methyl group about the C–C bond calculated by different methods: CNDO; extended Hückel method.

Nevertheless, calculations by the CNDO method by no means always give even qualitative agreement with experiment. Fig. 1 illustrates the variation in the total energy of the propionaldehyde molecule with the dihedral angle φ. Microwave[103] and nuclear magnetic resonance[104] spectra have shown the presence of two stable conformers differing in energy by 0.9 kcal mole^{-1}. The more stable conformer corresponds to $\varphi = 49°$, and the barrier separating them is 2.28 kcal mole^{-1}. The CNDO/2 method with Pople and Segal's parameters does not predict the existence of two conformers at all, quite apart from the position of the minimum[102]. In this case the extended Hückel method—which is considerably cruder than CNDO—yields better agreement with experiment.

In all the above examples the energy of internal rotation was calculated with bonds and valency angles fixed at values taken from experiment. This raises the question whether agreement with experiment could not be improved by basing the calculations on the optimum geometry, i.e. by requiring that the energy should be optimised with respect to bond lengths and valency angles for each angle of rotation. This question has been too little investigated for an unambiguous answer to be possible. We note merely that calculation with optimisation of the geometry for the hydrogen peroxide molecule gives two barriers—*cis* and *trans*—with energies of 5.0 and 2.85 kcal mole^{-1} respectively (in non-empirical calculations the *trans*-barrier can be predicted only with large basis-sets). Minimum energy corresponds to an angle of rotation of 87° read from the *cis*-form (the experimental angle is 111.5°).

The CNDO method makes it possible to understand which interactions are responsible for the appearance of barriers. The energy of interaction of the atoms E_{AB} (Eqn. 45) can be written as the sum of three components:

$$E_{AB} = E^{(1)}_{AB} + E^{(2)}_{AB} + E^{(3)}_{AB}, \tag{53}$$

where

$$E^{(1)}_{AB} = 2\sum_{\mu}^{A}\sum_{\nu}^{B} P_{\mu\nu}S_{\mu\nu}\beta^{0}_{AB} \tag{54}$$

$$E^{(2)}_{AB} = -\frac{1}{2}\sum_{\mu}^{A}\sum_{\nu}^{B} P^{2}_{\mu\nu}\gamma_{AB} \tag{55}$$

$$E^{(3)}_{AB} = P_{AA}P_{BB}\gamma_{AB} - P_{AA}Z'_{B}\gamma_{AB} - P_{BB}Z'_{A}\gamma_{AB} + Z'_{A}Z'_{B}/R_{AB} \tag{56}$$

and V_{AB} in (45) has been replaced by formula (47) in conformity with the CNDO/2 approximation.

The component $E^{(1)}_{AB}$ represents the main contribution to the energy of bonding made by the atomic orbitals $\varphi\mu$ and $\varphi\nu$ belonging to atoms A and B respectively. Since $\beta^{0}_{AB} < 0$, the inequality $E^{(1)}_{AB} < 0$ implies that this type of interaction between atoms A and B strengthens the bonding; the inequality $E^{(1)}_{AB} > 0$ corresponds to a weakening of bonding.

The component $E^{(2)}_{AB}$ represents stabilisation by exchange interactions.

Finally, $E^{(3)}_{AB}$ is the electrostatic interaction of atoms A and B, since

$$P_{AA} = \sum_{\mu}^{A} P_{\mu\mu}$$

is the total electron density on A. If at large distances $\gamma_{AB} \simeq 1/R_{AB}$, we actually have

$$E^{(3)}_{AB} = (P_{AA} - Z'_{A})(P_{BB} - Z'_{B})/R_{AB} = q_{A}q_{B}/R_{AB} \tag{57}$$

where q_A and q_B are the net charges of atoms A and B: i.e. Eqn. (57) corresponds to purely Coulombic interaction.

The energy E_A introduced by the orbitals of atom A (Eqn. 44) makes a very small contribution to the relative conformational energy. Thus for ethane, methylamine, and methanol $\Sigma_A \Delta E_A$ is respectively 0.08, 0.12, and 0.16 kcal mole^{-1}, and stabilises the eclipsed conformations[99].

Analysis shows[99] that in most cases the term $\Delta E^{(1)}_{AB}$ plays by far the major part in determining the barrier to internal rotation. In ethane, its fluorinated derivatives, methylamine, and methanol the barrier is due to H...H interaction (characterised by the parameter $E^{(1)}_{HH}$) in the eclipsed conformations. The electron density in the space between the hydrogen atoms is small, which leads to their repulsion. In the hydrazine molecule interaction of the lone pairs of the nitrogen atoms prevails over H...H repulsion. In molecules having large excess charges, such as hydroxylamine, the electrostatic contribution $\Delta E^{(3)}_{AB}$ plays an important part as well as $\Delta E^{(1)}_{AB}$.

The nature of the barriers in the hydrogen peroxide molecule is interesting. It is not surprising that H...H interaction, characterised by the parameter $\Delta E^{(1)}_{HH}$, is responsible for the *cis*-barrier. The *trans*-barrier is due mainly to interaction of π-electrons in the non-planar conformations, and is determined by the parameter ΔE_{OO} of the oxygen atoms. These characteristics of interatomic interaction appear only in calculations with optimisation of the geometry: if the experimental bond lengths and HOO valency angle are used, however, the minimum total energy will correspond to the *trans*-form.

Nevertheless, a more reliable assignment of the "nature" of the barriers to internal rotation in molecules can be obtained only on the basis of non-empirical calculations. Indeed, the neglect of many integrals and the replacement of a further series of integrals by empirical

parameters lead firstly to considerable errors in the calculated barriers and secondly to incorrect assessment of the effects of particular factors. Yet even an extremely rough non-empirical calculation (with a small basis-set) yields in most cases a correct idea of the relative importance of various contributions to the barrier. And still, independently of the method of calculation used, a fundamental difficulty arises in interpreting the "nature" of the barriers, because quantum-mechanical integrals can be combined in various groups in quite a number of ways, so that the interpretation will depend on the grouping adopted in a specific calculation.

The resolution of E_{AB} into components—$E_{AB}^{(1)}$, $E_{AB}^{(2)}$, and $E_{AB}^{(3)}$—enables us to understand why the extended Hückel method often gives reasonable conformational energies and barriers to internal rotation, while being completely unsuitable for calculating the geometry and the force constants of polyatomic molecules. Since the effective Hamiltonian of this method contains only terms proportional to $S_{\mu\nu}$, while ionisation potentials are used as diagonal elements, only the components E_A and $E_{AB}^{(1)}$ are taken into consideration, the remaining components being absorbed in empirical parameters. But the equilibrium geometry of the molecule is determined from the condition that the derivatives $\partial E/\partial x_i$ should vanish, where the x_i are independent geometric parameters, while the force constants $K_{ij} = \partial^2 E/\partial x_i \partial x_j$ are second derivatives. The contribution of electrostatic interaction $E_{AB}^{(3)}$ to these derivatives is, however, quite large, as estimates by Fisher and Kollmar[105] have shown. In many cases, therefore, calculation of molecular geometry and force constants by the extended Hückel method does not lead to the end in view.

The CNDO method, because of the presence of a large number of empirical parameters, is extremely flexible, and with appropriate choice of parameters may give good agreement with experiment. In fact, several successful attempts have been made to vary the parametrisation[106-117], especially in calculations of the geometry and the atomisation energies of hydrocarbons.

Table 5. Pople–Segal and Wiberg parameters for CNDO method.

Orbital	Core charge	Slater exponent	Ionisation potential, eV		β^0	
			P-S	W	P-S	W
1s H	1	1.2	7.1761	7.176	9	10.0
2s C	4	1.625	14.051	10.3	21	17.5
2p C		1.625	5.572	6.3		

Too profound significance should not be attached to calculations of energies of atomisation, of course, since correlation corrections amount numerically to an average 20% of the total energy. The LCAO-MO method in Roothaan's approximation does not predict the existence of the F_2 molecule at all[118], contrary to experimental results; in most cases, however, the existence of the equilibrium conformation is correctly predicted, but the calculated bond energies differ greatly from the true values. The same must be expected for the CNDO method, since it is a simplification of the Hartree–Fock model.

For certain homologous series, in particular for hydrocarbons, however, effective parameters can be so chosen that the calculated atomisation energies agree quite well with the experimental values.

Wiberg showed[117] that results calculated by the CNDO method are very sensitive to the proportionality constants β^0 and the mean ionisation potentials of the orbitals. Table 5 compares Pople and Segal's parameters with those of Wiberg. The slight difference in the constants β^0 for carbon atoms (17.5 instead of 21) permits considerable improvement in predicting molecular geometry. In fact, Table 6 shows that the calculations give bond lengths accurate to about 0.02–0.03 Å, and valency angles to 1–2°.

Table 6. Geometry of hydrocarbon molecules calculated by CNDO/2 method with Wiberg's parameters.

Molecule	Bond	Bond length, A		Angle	Angle, degrees	
		calc.	expt.		calc.	expt.
Methane	C—H	1.124	1.085			
Ethane	C—H	1.128	1.096	HCC	111.5	110.5
	C—C	1.506	1.531			
Propane	C—C	1.513	1.526	CCC	113.3	112.4
				HCH	105.6	106.1
Ethylene	C—H	1.120	1.076	CCH	123.3	122.2
	C=C	1.356	1.330			
Benzene	C...C	1.423	1.397			
Acetylene	C—H	1.103	1.061			
	C≡C	1.239	1.203			
Allene	C—H	1.120	1.082	CCH	122.8	120.2
	C=C	1.342	1.312			121.5

Table 7. Comparison between experiment and atomisation energies calculated by CNDO method (all energies in kcal mole^{-1}).

Molecule	$-\Delta E_{at}$, calc.	Zero-point vibrations	$-\Delta H_{at}$, expt.	$-\Delta E_{at}$, expt.*
Methane	419.61	27.11	392.86	419.97
Ethane	713.60	45.18	667.02	712.20
Propane	1006.91	62.46	943.61	1006.07
Butane	1298.62	79.77	1221.43	1301.20
Ethylene	563.14	30.70	532.74	563.44
Benzene	1373.14	62.84	1308.06	1370.90
Allene	710.44	33.23	672.95	706.18
Acetylene	416.33	16.18	389.69	406.50

*Allowing for zero-point vibrations.

Varying the mean ionisation potentials of the orbitals (Table 5) enables quite satisfactory agreement to be attained between calculated and experimental atomisation energies. It is noteworthy that comparison with experiment is based not on the enthalpies (as is mostly done) but on the atomisation energies: i.e. the zero-point vibrational energies of the atoms (Table 7, column 3) are added to the experimental enthalpies with their sign reversed. In order to obtain agreement with experiment (column 5), however, the calculated atomisation energies ΔE_{at} were treated by the method of least squares, to give the relation

$$-\Delta E_{at}(\text{kcal mole}^{-1}) = 218.01[-\Delta E_{at}(\text{a.u.})] + 35.28. \quad (58)$$

The right-hand side of this equation contains atomisation energies found by the CNDO method in atomic units, and the left-hand side the atomisation energies that are to be compared with the experimental values. Equation (58) is clearly not simply a conversion from one type of unit to another. It is a purely empirical relation, which governs the predictive value of the CNDO method with appropriate parametrisation.

As in any semi-empirical method, successful choice of parameters in the CNDO method permits the prediction of many—but by no means all—properties of molecules. Thus Wiberg's parametrisation gives strongly underestimated barriers to internal rotation: the calculated barrier in ethane is only 0.7 kcal mole^{-1}. While yielding good agreement with experiment for atomisation energies, this parametrisation does not give reliable values for the energies of individual bonds, and therefore has recently been re-examined by Ehrenson and Seltzer[119].

As already mentioned, Pople and Segal's original parametrisation, while not leading to agreement with experiment for molecular geometry and atomisation energies, nevertheless indicates the changes in barriers to internal rotation occurring on passing from one molecule to another, although the calculated numerical values are usually considerably lower than the experimental values. In cases in which the barriers in π-electron systems are due mainly to repulsion of non-bonded atoms, however, the CNDO method does not give results agreeing with experiment. Thus a calculation for biphenyl showed[120] that the total energy does not pass through a minimum as a function of the dihedral angle between the phenyl rings, although such a curve should have a minimum at $\sim 40°$. The CNDO method also gives incorrect relations between total energy and equilibrium angle of deflection of the phenyl rings[121] for *cis*- and *trans*-stilbenes: they do not agree with the curves obtained from empirical potential functions and do not lead to equilibrium structures comparable with the results of X-ray diffraction; the calculated barrier to the *cis–trans* isomerisation of stilbene is too high—129 instead of the experimental 43 kcal mole^{-1}.

The above examples of the application of the CNDO method force us to treat the calculated results with caution, especially in the case of energy differences. An attempt to predict the mechanism of the *cis–trans* isomerisation of the difluorodi-imide molecule[122] is interesting in this connection. Both forms (Fig. 2) are stable at room temperature, and their structures have been established by detailed investigations[123,124]. Calculations by the CNDO method showed that they actually corresponded to energy minima, with the *cis*- more stable than the *trans*-form by 4.5 kcal mole^{-1} (the experimental energy difference is 3.0 kcal mole^{-1}). The geometry corresponding to the energy minima is not entirely consistent with experiment: the N=N bond length coincides with the experimental value, but the N–F bond is 0.15 Å shorter (calculated and experimental values 1.26 and 1.41 Å); the calculated valency angles differ from the experimental by 2–3°.

Two routes are obviously possible for *cis–trans* isomerisation in this compound: (i) an N–F bond may "bend back", when the transition state will correspond to a configuration in which the two nitrogen atoms and one fluorine atom lie on a straight line (Fig. 2); (ii) rotation about the N=N bond will give a transition state in which the two F–N=N planes are mutually perpendicular. Calculation gives saddle-point energies respectively of 75 and $\sim$ 80 kcal mole^{-1} for the two paths. However, the experimental kinetic equation[125] is $k = 10^{14} \exp[-32.2\ (\text{kcal})/RT]\ \text{s}^{-1}$. Thus the CNDO method gives an activation energy that is inconsistent with experiment. Since the calculated energies of the transition states were almost identical, however, no preference could be made for either mechanism in this example.

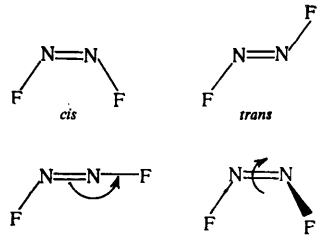


Figure 2. Stable and transitional forms of the difluorodiimide molecule.

The CNDO method bred a whole family of conceptually closely similar semi-empirical methods. Among them may be mentioned the neglect of diatomic differential overlap (NDDO) and partial (intermediate) neglect of differential overlap (INDO). The NDDO method, suggested long ago by Pople et al.,[31] neglects diatomic differential overlap while retaining integrals with the products $\varphi_\mu\varphi_\nu$ for different orbitals on the same atom. The INDO method[33] retains all one-centrel exchange integrals, while neglecting the remaining two-electron integrals. Finally, mention must be made of a few methods "terminating in differential overlap" and occupying a position intermediate between CNDO, NDDO, and INDO[97,98,126–136].

Among all the methods of zero differential overlap, NDDO is the closest approximation to the Roothaan equations[31,137]. The serious defects of NDDO must include the difficulty of parametrisation and the long computer time required. In a detailed examination of the possibilities of this method[101] the parameters β^0 were chosen to give agreement between calculated and experimental bond lengths and valency angles in hydrocarbons. This yielded a geometry agreeing satisfactorily with experiment: deviations in carbon–carbon bond lengths were on the average 0.01 Å and in carbon–hydrogen bond lengths 0.04 Å. But the barriers to internal rotation calculated with the same parameters were unsatisfactory: whereas the CNDO method underestimated all barriers, but gave the correct trend for variations from molecule to molecule, even the trend becomes blurred in the NDDO method. Energies of isomerisation (isobutene → *trans*-but-2-ene → *cis*-but-2-ene; isobutane → n-butane) disagree with experiment even in sign. Thus the introduction of additional integrals into the CNDO method not only does not improve but rather impairs the agreement with experiment. However, such a situation is typical of many semi-empirical methods, and was encountered repeatedly during the period of flowering of π-electron approximations.

The INDO method also does not improve (but does not worsen) the agreement with experiment. Table 8 gives bond lengths and valency angles calculated by this method[138] for several molecules. Comparison with Table 3 shows that, for ethane, methanol, hydrogen peroxide, and dioxygen difluoride, use of a more rigorous approximation has

hardly any effect on the molecular geometry. The impression is produced that optimisation of the parameters of a method is more effective for predicting geometry than are further complications of the theory.

Table 8. Geometry of molecules calculated by INDO method.

Molecule	Bond	Bond length, Å		Angle	Angle, degrees	
		calc.	expt.		calc.	expt.
NH_3	N—H	1.07	1.02	HNH	106.4	109.1
NF_3	N—F	1.25	1.37	FNF	104.4	102.2
CH_4	C—H	1.12	1.09			
CF_4	C—F	1.34	1.32			
H_3COH	C—O	1.37	1.43	COH	107.3	105.9
	C—H	1.12	1.09	HCH	108.2	109.5
	O—H	1.04	0.94			
$H_3C—CH_3$	C—C	1.46	1.53			
	C—H	1.12	1.10	HCH	106.6	107.8
$F_3C—CF_3$	C—F	1.35	1.33	FCF	106.1	108.0
	C—C	1.45	1.51			
HO—OH	O—O	1.22	1.47	HOO	108.8	94.8
	O—H	1.04	0.95	∠φ	83.5	111.5
FO—OF	O—O	1.23	1.22	FOO	108.4	109.5
	O—F	1.19	1.57	∠φ	85.8	87.5

Table 9. Comparison between experiment and energies of formation ΔHform (at 298°K) of cyclic hydrocarbons calculated by MINDO/1 method[129].

Molecule	Heat of formation		Molecule	Heat of formation	
	MINDO/1	expt.		MINDO/1	expt.
Cyclopropane	16.36	12.72	Bicyclo-butane	52.29	51.9
Cyclobutane	11.34	6.35	Cyclopentene	8.11	7.73
Cyclopentane	−19.23	−18.46	Cyclopentadiene	30.16	32.44
Cubane	116.88	148.70			

Special consideration must be given to the MINDO (modified INDO) method proposed by Dewar and his coworkers[129-131]. The main idea of MINDO/1 consisted in selecting empirical parameters designed to reproduce experimental heats of formation of organic molecules from the atoms. This involved the parametrisation of many integrals. Since, however, computer time is mainly devoted to evaluating quantum-mechanical integrals, the MINDO method enabled the duration of the calculation to be shortened by more than 90% in comparison with CNDO. In the MINDO/2 variant[131] the parameters were chosen to obtain agreement with experiment not only for energies of formation but also for the molecular geometry. As a result, the accuracy with which heats of formation could be predicted for most organic molecules became about ±2–3 kcal mole^{-1}, and the accuracy of calculating bond lengths and valency angles ±0.01 Å and ±2–3° respectively. Because of its great accuracy the MINDO method is widely employed[139-144] for calculating geometry, barriers to rotation around bonds, and thermochemical properties of organic molecules, as well as for investigating the paths of organic reactions.

Table 9 lists heats of formation calculated for several cyclic and polycyclic hydrocarbons (by the MINDO/1 variant, which for thermochemical properties gives better agreement with experiment than does MINDO/2). These results show about the same agreement with experiment as in calculations using the interatomic potential model[13,145,146]. This is not surprising, however, for in the MINDO method quantum mechanics has already been brought down almost to the level of empirical models: the parameters of the method are very far from reproducing non-empirical calculations (and this was the idea of parametrisation in the CNDO method); on the other hand, they are very valuable for the chemist who wishes to predict with great accuracy the structures and the properties of complicated organic systems.

VI. APPLICATION OF LOCALISED ORBITALS IN SEMI-EMPIRICAL CALCULATIONS

Hitherto we have been examining methods based on delocalised molecular orbitals, each of which is a linear combination of atomic orbitals. It was precisely from them that the Slater determinant (6) was constructed. However, such a determinant can be constructed also on the basis of localised molecular orbitals, in particular those of valency bonds, representing the stereochemical character of the molecule. If functions set up from hybrid atomic orbitals (of types sp^3, sp^2, and sp) are chosen as these localised molecular orbitals, and the coefficients representing the hybrid state are fixed, there is no need to use the Hartree–Fock equations and hence a self-consistency procedure. Such a mode of action is not very good with a non-empirical approach, of course, for the resulting accuracy is too low. In calculations *ab initio*, therefore, the coefficients of hybrid orbitals are optimised by a variational method. Molecular orbitals of methane, for example, can be sought in the form[147]

$$i = A(i_1 + \lambda i_2) \qquad (59)$$

where i_1 is the hybrid tetrahedral orbital of carbon directed towards one of the hydrogen atoms, i_2 is a 1*s* orbital centred on the same hydrogen atom, and A is a normalising factor. The parameter λ can be optimised with respect either to the length of the carbon–hydrogen bond (to make the calculation coincide with experiment) or to some other property.

In semi-empirical methods, however, whose accuracy depends significantly on the parametrisation, it hardly makes sense to proceed in this way: the use of pure hybrid orbitals seems more promising, and then the total energy can be calculated without the need for variational procedures, resulting in a considerable saving of time in comparison with self-consistent methods of the zero differential overlap type.

The principal disadvantage of localised orbitals is that the wave function based on them differs significantly from that of the self-consistent field, while the total energy is far from the Hartree–Fock limit. However, by the use of localised orbitals together with a method of "interaction" of configurations, we can go far beyond the scope of the Hartree–Fock approximation and obtain a considerable proportion of the correlation energy due to "instantaneous" interactions of the electrons[148,149]. This represents a considerable advantage of localised molecular orbitals over delocalised LCAO-MO orbitals.

French workers[150] have used perturbation theory to develop a technique for computing the total energy of a molecule. The Slater determinant, constructed from bonding orbitals completely localised on the bonds, is regarded as a wave function of zero order. Antibonding

orbitals are used to construct wave functions of excited states, and a matrix of configurational "interactions" is based on such functions (configurations). The theory of perturbations is then used to find the energy and the eigenfunction of the ground state.

We shall consider in greater detail the above procedure for systems having closed electron shells (even number N of electrons). Let i and i^* be the bonding and the antibonding orbital corresponding to the ith bond, which can be represented by a linear combination of the hybrid orbitals i_1 and i_2:

$$i = \alpha i_1 + \beta i_2, \tag{60}$$

$$i^* = \beta' i_1 - \alpha' i_2. \tag{61}$$

We assume the localised molecular orbitals (60) and (61) to be known (they can be found, for example, from Hartree–Fock calculations of small molecules). The zero-order wave function can then be written as a Slater determinant:

$$\Psi_0 = (1/2n!)^{1/2} |1\bar{1} \ldots i\bar{i} \ldots n\bar{n}|, \tag{62}$$

which coincides with (6) as $n = \frac{1}{2}N$. The energy of this wave function is calculated as the average value of the Hamiltonian H.

We now consider singly excited configurations, by promoting one electron from the orbital i to the antibonding orbital j^*, and also doubly excited configurations, by promoting electrons from orbitals i and k to antibonding orbitals j^* and l^*:

$$\Psi(\bar{j}_i^*) = (1/\sqrt{2n!})^{1/2} |1\bar{1} \ldots i\bar{j}^* \ldots n\bar{n}|, \tag{63}$$

$$\Psi\left(\frac{\bar{j}^*\bar{l}^*}{ik}\right) = (1/\sqrt{2n!})^{1/2} |1\bar{1} \ldots i\bar{j}^* \ldots k\bar{l}^* \ldots n\bar{n}|. \tag{64}$$

Using the methods of perturbation theory, it was shown[150] that the approximate wave function Ψ and the energy E are given by the formulae

$$\Psi \cong \Psi_0 + \sum_{i,j^*} \frac{\left\langle \Psi_0 | H | \Psi_0 \left(\frac{j^*}{i}\right) \right\rangle}{E_0 - E(j_i^*)} \Psi(j_i^*) + \sum_{i,k,j^*,l^*} \frac{\left\langle \Psi_0 | H | \Psi \left(\frac{j^*l^*}{ik}\right) \right\rangle}{E_0 - E\left(\frac{j^*l^*}{ik}\right)} \Psi\left(\frac{j^*l^*}{ik}\right) \tag{65}$$

$$E \cong \langle \Psi_0 | H | \Psi_0 \rangle + \sum_{i,j^*} \frac{\left\langle \Psi_0 | H | \Psi_0 \left(\frac{j^*}{i}\right) \right\rangle^2}{E_0 - E\left(\frac{j^*}{i}\right)} + \sum_{i,k,j^*,l^*} \frac{\left\langle \Psi_0 | H | \Psi \left(\frac{j^*l^*}{ik}\right) \right\rangle}{E_0 - E\left(\frac{j^*l^*}{ik}\right)}, \tag{66}$$

where it is a simple matter to calculate $E(j^*/i)$ and $E(j^*l^*/ik)$. If the approximation of zero differential overlap is now applied, i.e. if n^4 integrals of type $(ij|j^*i^*)$ present in formulae (65) and (66) are equated to zero, it only remains to evaluate n^2 integrals of type $(ij|i^*j^*)$. But the main gain in time of calculation is due to the absence of a self-consistency procedure.

The above method has been termed perturbative configuration interaction using localised orbitals (PCILO). In practical application, this method is usually confined to a minimal basis-set of localised bond orbitals. Thus four bonding and four antibonding carbon–hydrogen orbitals are considered for ethylene, together with σ- and π-orbitals of the C=C bond. Not only valency orbitals but also 1s orbitals of the inner shells are included. Since the number of integrals is large, although considerably smaller than in methods of configurational interactions based on Hartree–Fock LCAO-MO, the method is usually restricted to zero differential overlap by the use of CNDO/2 parametrisation.

The great merit of the PCILO method with CNDO parametrisation is the comparatively short time of computation: the total energy of a molecule, allowing for a considerable proportion of correlation energy, is calculated on an electronic computer in roughly the time required to calculate empirical potential functions or total energy in the extended Hückel method. This makes PCILO suitable for solving relatively complicated conformational problems. Pullman and his coworkers have employed the PCILO method to construct conformational maps of dipeptides[151–156], to investigate the conformations of conjugated systems playing an important part in the mechanism of visual stimulation[157,158], to calculate the relative energies of steroid systems[159], and to make conformational analyses of disaccharides[160].

Although the PCILO method is in principle more accurate than the Hartree–Fock LCAO-MO method, it is still difficult to state whether it yields more reliable calculated geometric parameters and conformational energies. Even with restricted basis-sets Hartree–Fock calculations *ab initio* lead to an entirely reasonable geometry and reasonable barriers to internal rotation[161,162]. Hence correlation need not in general be taken into account. But it is not excluded that the introduction of correlation corrections into CNDO/2 may lead to an improvement of this semi-empirical method.

Certain results of calculations of simple molecules may give an idea of the possibilities of the PCILO method. Barriers to internal rotation calculated[151] for formamide, acetamide, *N*-methylformamide, and *N*-methylacetamide, respectively 20.8, 14.3, 13.1, and 12.8 kcal mole^{-1}, were close to the experimental values: for formamide, in particular, the experimental values lay in the range 16.8–21.9 kcal mole^{-1}[163–165], and those calculated *ab initio* in the range 19.4–24.7 kcal mole^{-1}[166,167]. In this case the PCILO method based on CNDO/2 parametrisation will give the correct height of the barrier (20.8 kcal mole^{-1}), whereas use of the CNDO/2 method in its original form usually underestimates the barriers.

Calculation of conformational energies for such classical systems as cyclohexane, cyclopentane, and decalin has given interesting results[159] (all values in kcal mole^{-1}): in cyclohexane the boat is less stable than the chair by 5.8 (the experimental energy difference is ~ 6); in cyclopentane the half-chair is more stable than the envelope by 0.7 (this result is not entirely satisfactory, as pseudorotation occurs in cyclopentane almost without hindrance[81]); and *trans*-decalin is more stable than the *cis*-isomer by 2.0 (experimental energy of isomerisation 2.7[168]). Further, calculated values[169] of the barrier to internal rotation in propene are 1.31 with second-order perturbation and 1.22 with third-order perturbation (experimental value 1.98[100]). In methylketen $CH_3.CH:C:O$ the calculated barrier to rotation of the methyl group is 1.54 and 1.31 with second- and third-order perturbation respectively (experiment gives 1.18[100]).

Langlet and van der Meer compared the results obtained by calculating the geometry of ethylene, propene, keten, and methylketen by the extended Hückel[170] and PCILO[169] methods. All calculations were made with fixed bond lengths taken from experiment; the ultimate aim was to find valency angles satisfying minimum total energy (such a procedure is not entirely systematic, of course: in principle a minimum should properly be sought with respect to all parameters). Neither method gave satisfactory results. For the H–C=C angle in methylketen, in particular, the extended Hückel method gives a value of 121.4°, and PCILO yields 119.2° and 117.3° with second- and

third-order perturbation respectively. These three values exceed considerably the experimental angle of 113.7°.[171]

Althqugh the PCILO method has been tested only on a small number of simple molecules, it has become clear that, like any semi-empirical method, it may suffer from the imperfections of parametrisation. The rôle of correlation corrections in the PCILO–CNDO/2 scheme has not yet been finally elucidated, and therefore it is at present difficult to know whether the PCILO method is to be preferred to the classical form of CNDO/2. Nevertheless, in contrast to the latter, the PCILO method makes it possible to calculate in a comparatively short time the relative energies of a multitude of conformations of extremely complicated molecules such as dipeptides and disaccharides. This is the chief merit of the new method.

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Summing up, we can state that the semi-empirical methods examined in this Review—extended Hückel method, CNDO, MINDO, PCILO, and certain others—are undoubtedly useful for comparative estimates of the properties of polyatomic molecules. However, the results obtainable by semi-empirical methods depend on the parametrisation adopted, and therefore are not always reliable. In this sense calculations *ab initio* have an undoubted advantage.

But it must not be thought that non-empirical calculations will be able in the forseeable future to replace semi-empirical methods of quantum chemistry completely. Organic molecules of interest to chemists are usually too large for their geometry and conformational energies to be estimated by evaluating all the quantum-mechanical integrals. It is also difficult to envisage the possibility of minimising the Hartree–Fock functional with respect to independent geometric parameters: for molecules of moderate size such a procedure would require an unreasonably long computer time. Yet problems of seeking the equilibrium geometry and calculating conformational energies are easily solved by empirical and semi-empirical methods. This is why such methods, it must be assumed, will acquire still greater popularity among wide circles of chemists.

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Institute of Organoelementary Compounds,
USSR Academy of Sciences, Moscow

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Separation of Liquid Organic Mixtures by Diffusional Permeation Through Non-porous Polymer Membranes

A.A.El'bert

The physicochemical aspects of a new method of separation of organic liquids by diffusional permeation through non-porous polymer membranes are discussed. The process is assumed to consist of 5 successive steps: transport of material from the liquid to the membrane surface, sorption by the surface layer of the membrane, diffusion through the membrane, desorption from the opposite side of the membrane, and evaporation of the desorbed molecules into the gas (or vapour) phase. The influence of the polymer structure (polyethylene, polypropylene) on the separation process is discussed, and possible modifications of the membrane by solvent treatment, unidirectional mechanical stress, cross-linking by radiation-chemical and photochemical methods, and grafting of other polymers are considered. The effects of the composition of the initial mixture, of the nature of the compounds to be separated, and of temperature are also discussed.

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I. INTRODUCTION

Separation processes are extremely important in the chemical industry. New and increasingly complex problems concerning the separation of mixtures are often encountered, which traditional methods (fractional distillation, adsorption, absorption, fractional freezing, extraction) are powerless to solve. New methods of separation have therefore been proposed and developed, such as counter-current crystallisation, preparative chromatography, separation by ion-exchange resins and molecular sieves, and gel chromatography.

Separation by permeation through membranes is one of these newer methods. All variants of this technique rely on the selective transfer of materials through a semipermeable partition. The driving force of the process can be a temperature gradient, a concentration gradient, or a pressure gradient. Some processes use polymer membranes (reverse osmosis, ultrafiltration, diffusional permeation), others use porous glass or metal membranes, or metal foils. The nature of the processes within the membrane can vary quite considerably. For example, the separation of hydrogen by palladium alloy membranes relies on the unique properties of the palladium crystal lattice; ultrafiltration processes rely on the properties and on the molecular size of substances dissolved in water; separation by means of porous glasses depends almost entirely on the size of the solute molecules.

It is clear, from recent review articles dealing with various separation methods based on membranes[1-11], that diffusional permeation through non-porous polymer membranes is the method most widely used for separating mixtures of liquid organic compounds. The separation of organic liquids by ultrafiltration under high pressure (up to 100 kg cm^{-2}) through porous polymer membranes is unacceptably slow, and is complicated by irreversible changes in the membrane during operation[12,13].

We shall therefore confine our discussion to the separation of organic mixtures by diffusional permeation through non-porous polymer membranes. In the Western literature this method of separation is usually termed "permeation" or (less frequently) "pervaporation". The principle of the method, the essential differences from other methods of separation, and possible applications on an industrial scale were first discussed between the late 1950's and the early 1960's[14-18].

This review aims to explain (on the basis of published data) the main features of this method of separation and to assess the influence of various factors on the rate of permeation of materials through a membrane and on the selectivity of the separation process.

II. FIVE-STAGE MECHANISM FOR THE PERMEATION OF SUBSTANCES THROUGH THE MEMBRANE

The separation of substances by permeation through polymer membranes is carried out as follows: the liquid mixture, heated to the required temperature, is placed in contact with a thin polymer membrane (usually 50 to 100 μm thick). The material which passes through the membrane is removed by pumping or in a stream of inert gas. The permeation of a liquid through a membrane consists of the following 5 steps: 1) transfer of material from the centre of the liquid flow to the surface of the membrane, 2) sorption by the surface layer of the membrane, 3) diffusion through the membrane, 4) desorption from the opposite surface of the membrane, 5) transfer from the desorption layer of the membrane surface to the gas (or vapour) phase.

It is not always possible to resolve all 5 stages: for example, stages 1 and 2, and also 4 and 5, are sometimes combined by adding their resistances[19,20].

In order to simplify the terminology we shall assume that the membrane is located horizontally, and that its upper surface is in contact with the liquid and its lower surface with the vapour. We begin with a discussion of the 5 individual stages, and of the way in which each stage affects the overall process.

1. Transfer of Material from the Centre of the Liquid Flow to the Surface of the Membrane

This stage consists essentially in the transport of matter and heat to the surface of the membrane. It has fundamental significance both in the permeation of pure substances, when concentration polarisation cannot arise†, and in the separation of multicomponent mixtures. Hence, vigorous stirring of the liquid is advisable, as was suggested in some of the early papers[21-23]. A more recent paper[24] shows that the rate of permeation can be raised very considerably by increasing the speed of the stirrer.

It is stated[21-23] that a Reynolds number in the liquid of 2300 is sufficient to bring the resistance of stage 1 to a minimum. However, this conclusion may be true only for rates of permeation below 10 kg m^{-2} h^{-1}, and should be tested experimentally at the higher mass flows currently of interest (up to 50–60 kg m^{-2} h^{-1}).

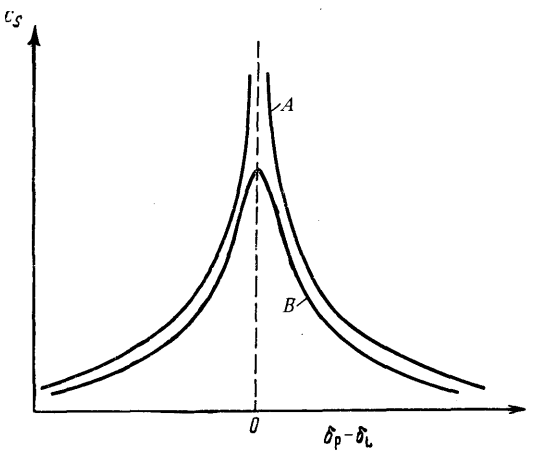


Figure 1. Influence of the Hildebrand solubility parameter on the solubility of liquids in a polymer: δ_p is the solubility parameter of the polymer, δ_L is the solubility parameter of the liquid, *A* is the curve for a linear amorphous polymer, *B* is the curve for a cross-linked or crystalline polymer.

2. Sorption by the Surface Layer of the Membrane

Sorption of the liquid by the polymer membrane is an essential step in the process, because substances which are not sorbed by the membrane (i.e. which are insoluble in it) are incapable of permeation. The dissolution of a liquid in a polymer is described by the Hildebrand solubility parameter. The smaller the difference between the solubility parameters of the liquid and of the polymer, the greater is the solubility (see Fig. 1).[10,25-28] For example, the solubility parameter δ for polyethylene is 7.7–8.4 $(cal\,cm^{-3})^{1/2}$, and for benzene and n-hexane, which are readily soluble in polyethylene, the parameter is 9.2 and 7.3 respectively (all values for 25°).[27]

Long[29] suggested that an equilibrium is rapidly set up at the liquid–polymer interface during the permeation of toluene, methylcyclohexane, and n-heptane through polypropylene membranes. He writes $c_1 = c_S$, where c_1 is the concentration of the permeating substance in the upper layer of the membrane and c_S is the solubility of the permeating substance in the polymer. According to Long, the solubility of hydrocarbons increases with temperature, reaching values of 0.17, 0.23, and 0.34 g per g of dry polymer for n-heptane, toluene, and methylcyclohexane respectively at 60°. Kim and Kammermeyer[30] have measured the concentration profiles during permeation of organic liquids through membranes, and have compared their results with experimentally measured equilibrium concentrations of dioxan in Nylon and dioxan, n-hexane, and benzene in polyethylene. They report that the true concentration of the permeating substance in the upper layer of the membrane is close to (but slightly lower than) the equilibrium value.

Michaels and coworkers[31] measured the solubility of xylene isomers in high-pressure and low-pressure polyethylene: at 25° the solubility of *o*-, *m*-, and *p*-xylene in high-pressure polyethylene is 0.169, 0.136, and 0.118 g per g of dry polymer respectively.

An unsuccessful attempt to measure directly the sorption of liquid benzene by polyethylene membranes has been reported[32]: the results were erratic, and in some cases the membrane lost weight as a result of the extraction of some of its material by the benzene.

The difficulties attending direct experimental measurements of sorption equilibrium have been stressed by Paul[33], who proposed an indirect method of measuring c_S based on the "time-lag" method[34]. In this method, two separate experiments are made on the permeation of the same substance through the membrane: in one experiment, the permeation is monitored from the time when the dry membrane first makes contact with the liquid to the time when equilibrium is established, in the other experiment the permeation is monitored under steady-state conditions. Fick's second law equation had been previously solved for the special case of a concentration-independent diffusion coefficient[35], and also for the general case when the diffusion coefficient is a function of the concentration of the permeating substance in the membrane[33]. A mathematical analysis of the experimental results, using these equations, yields the required value of c_S.

Fels[36] has described an interesting method of measuring equilibrium sorption: by using an electro-balance, he determined c_S for n-heptane and cyclohexane vapours at different activities, and hence he calculated c_S for the liquids by extrapolation. The only drawback of this method is the very laborious experimentation involved.

As we have already pointed out, substances which are not sorbed by the membrane cannot be transmitted through it. However, an exception to this rule is possible, at least in principle: substances which in the pure form are very slowly transmitted through a given membrane may acquire a higher solubility in the membrane, and be readily transmitted, when mixed with other substances which can diffuse rapidly through the same membrane[37]. Effectively, the substance which is readily soluble in the polymer retains the ability to dissolve the substance which in the pure form is insoluble in the polymer, and is thus able to "entrain" it. Furthermore, a very soluble material can expand the structure of the polymer and plasticise

†Concentration polarisation is the increase in concentration of the less rapidly diffusing component, in the boundary layer of liquid adjacent to the surface of the membrane, observed with inadequate stirring.

it[3,10,25,26,37-41], thus assisting the migration of other substances through the membrane. The plasticising effect can be detected also when all the components of a mixture are readily sorbed by the polymer: the rate of permeation of the mixture is usually greater than the "additive" value, calculated from the composition of the mixture and the rates of permeation of the individual components[36,41-43]. The abnormally high rate of permeation of mixtures (benzene–n-hexane, benzene–cyclohexane, n-hexane–cyclohexane) through a polyethylene membrane is also explained[42] by assuming an increased activity of the components, resulting from intermolecular interaction, which enables the molecules to penetrate more readily into the polymer structure, thus raising the concentration of each component in the outermost layer of the membrane beyond the level corresponding to the permeation of an ideal mixture. A decrease in the activity of the components (and therefore in the rate of permeation) as compared with ideal behaviour is another possibility.

Thermodynamic calculation of the sorption isotherm is not possible at the present time, and therefore the isotherms must be determined experimentally.

The sorption of one liquid component is complicated to such an extent by the presence of another component that it is impossible, as a rule, to predict the sorption behaviour of a mixture from a knowledge of the data relating to the individual components. Values of c_1 applicable to the separation of binary and more complex mixtures by permeation through a membrane are not available in the literature.

3. Diffusion Through the Membrane

The third stage of permeation through a membrane is diffusion under the influence of the concentration difference between the upper and the lower surface layer or, more precisely, under the influence of the activity difference. The activity in the polymer can be calculated by the Flory–Huggins equation

$$\ln a_p = \ln V_p + (1 - V_p) + \chi(1 - V_p)^2 \qquad (1)$$

where a_p is the activity of the material dissolved in the polymer, V_p is its volume fraction in the polymer, and χ is the interaction parameter. According to existing data, χ is a function of temperature and concentration, but in most systems it varies over a narrow range (from 0.3 to 0.8). For example, for benzene and an ethylene–propylene copolymer $\chi = 0.65$, and for n-hexane and the same polymer $\chi = 0.3$;[44] for the benzene–polyethylene system $\chi = 0.68$–0.90;[45] for xylene and polyethylene $\chi = (-0.48 + 318/T) \pm 0.2$ where T is temperature in °K.[46]

If the swelling of the membrane in the permeating liquid is appreciable (over 1%) the diffusion coefficient D_c increases exponentially with the concentration of the liquid in the polymer, and the activation energy for diffusion E_{D_c} decreases linearly[10,25,26,28-30,36,47]:

$$D_c = D_0 \exp(\gamma c), \qquad (2)$$

$$E_{D_c} = E_{D_0} - \gamma' c. \qquad (3)$$

In these equations c is the concentration of the permeating substance in the membrane and γ and γ' are constants. As the concentration is increased, E_{D_c} can decrease by 10 kcal mole^{-1},[10] and D_c (in the case of hydrocarbon diffusion through polyethylene membranes) can increase from 10^{-11} to 10^{-7} cm^2 s^{-1}.[25,26,41]

Long[29] has determined experimentally the values of D_0 and γ in the equation

$$G = \frac{D_0}{\alpha l}(e^{\gamma c_s} - 1) \qquad (4)$$

for the permeation of toluene, methylcyclohexane, and n-heptane through polypropylene membranes. In this equation α is a constant and l is the thickness of the membrane. Eqn. (4) was derived on the assumption that Eqn. (2) applies, that $c_1 = c_S$, and that the concentration at the lower surface of the membrane is $c_2 = 0$. From his experimental results Long was able to calculate the concentration profile across the membrane.

Kim and Kammermeyer[30], starting from Fick's second law and assuming an exponential dependence of the diffusion coefficient on concentration (Eqn. (2)), obtained the following equations for calculating the concentration profile in the membrane and the diffusion coefficient applicable to the permeation of a liquid through a membrane (assuming $c_2 = 0$):

$$\frac{dc}{dl} = \left(\frac{1}{l}\right)^2 \frac{1 - e^{\gamma c_1}}{(1 - e^{\gamma c_1})\, l + e^{\gamma c_1}}, \qquad (5)$$

$$\frac{dD}{dl} = D_0(1 - e^{\gamma c_1}). \qquad (6)$$

In these equations $0 \leqslant l \leqslant 1$. The authors concluded that the diffusion coefficient decreases linearly across the thickness of the membrane, as required by Eqn. (6). The mean (effective) diffusion coefficient $\bar{D}$ is defined as

$$\bar{D} = \frac{D_0}{c_1} \int_0^{c_1} e^{\gamma c}\, dc. \qquad (7)$$

The assumption that $c_2 = 0$ is usually admissible when the space below the membrane is continuously evacuated.

Kim and Kammermeyer[30] measured the concentration profile across the membrane and the permeation of water and dioxan through Nylon membranes and n-hexane, benzene, and dioxan through polyethylene membranes (see Fig. 2). The experimental technique consisted in using a pack of 15–25 tightly pressed thin layers as the membrane; after the experiment the pack was dismantled and the concentration of the permeating substance in each layer was determined.

Experimental determinations of the diffusion coefficient followed by graphical analysis of the results by the "time-lag" method have been reported. The method relies on measurements of the penetration of liquid through the membrane from the instant when the liquid is brought into contact with the dry membrane[48,49]. The main shortcoming of this method, according to the authors themselves, is that the error in the calculated diffusion coefficient is always several times greater than the error in the experimentally measured rate of permeation.

Fels and Huang[50] measured the diffusion coefficient by observing desorption from previously swelled membranes. They modified Fick's second law for the assumption of "volume-additive" swelling, i.e. that the increase in volume of the polymer is uniquely determined by the dissolution of liquid in it (as had been previously confirmed experimentally for the dissolution of benzene and n-hexane in polyethylene[51]), and they arrived at the equation

$$\frac{dc}{dt} = \frac{\partial}{\partial l}\left[\frac{D_c}{(1 - V_p)} \frac{\partial c}{\partial l}\right]. \qquad (8)$$

They used this equation in their next paper, devoted to a theoretical interpretation of the effect of the initial composition of the mixture on the separation of benzene and

n-hexane by permeation through a polyethylene membrane[26]. We shall summarise their arguments below.

The theoretical approach of Fels and Huang[25,26,50] is based on Fujita's suggestion[52] that free volume is present within the polymer. This term is analogous to the concept of "holes" during thermal fluctuations, and denotes the total fraction of free volume in the polymer. The free volume is a function of temperature and of the concentration of solutes in the polymer, and can be presented in the form

$$f(V_p, T) = f(0, T) + \beta(T)V_p \quad (9)$$

where $f(V_p, T)$ is the free volume at given values of T and V_p, $f(0, T)$ is the free volume of the dry polymer, and $\beta(T)$ is a proportionality coefficient. When $V_p = 0$ we obtain the intrinsic free volume of the polymer, and when $V_p = 1$ the free volume of the diffusing substance. According to Fujita

$$\ln \frac{D_T}{D_c} = \frac{V_p}{[f(0, T)]^2/[B_d \cdot \beta(T)] + [f(0, T)/B_d] \cdot V_p} \quad (10)$$

where B_d is an arbitrary parameter corresponding to the smallest "hole" needed for diffusional transport, and D_T is the thermodynamic diffusion coefficient

$$D_T = \frac{D_c}{(1 - V_p)} \frac{\partial \ln V_p}{\partial \ln a_p} . \quad (11)$$

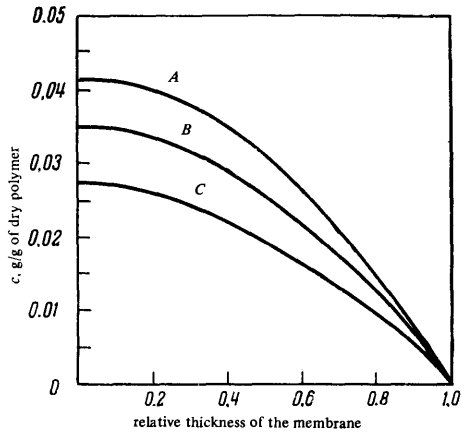


Figure 2. Concentration profiles during permeation of a liquid mixture through a membrane[30]. Membrane of high-pressure polyethylene, 0.0432 cm thick, separation temperature 35°, *A* is n-hexane, *B* is benzene, *C* is dioxan. c_S of the three components 0.043, 0.044, and 0.039 g/g of dry polymer respectively.

Michaels and coworkers[28] have measured, by two methods, the diffusion coefficient in polypropylene before and after treatment in a solvent at high temperature. (The effect of solvent treatment is discussed below.) The first method depends on calculating the rate of permeation (G) through the membrane by Fick's second law:

$$Q = \bar{D}_Q c_1 \quad (12)$$

where $Q = Gl$. Since the thickness of the membrane is constant, we can calculate $\bar{D}_Q$ from the experimentally measured quantities G and c_1 (assuming that $c_2 = 0$). The second method is a calculation based on experimental observations of sorption and desorption of the same substances by the membrane:

$$\bar{D}_a = \frac{\bar{D}_{abs.} + \bar{D}_{des.}}{2} \quad (13)$$

where $\bar{D}_{abs.}$ is the mean diffusion coefficient determined from absorption experiments, and $\bar{D}_{des.}$ is determined from desorption experiments.

Table 1. Comparison of diffusion coefficients obtained from membrane permeation experiments (Eqn. (12)) and from sorption–desorption experiments (Eqn. (13))[28]. $T = 40°$.

Permeating substance	$10^7\bar{D}_Q$, cm^2 s^{-1}			$10^7\bar{D}_a$, cm^2 s^{-1}		
	polypropylene membrane, untreated	polypropylene membrane treated 24 h in *p*-xylene at		polypropylene membrane, untreated	polypropylene membrane treated 24 h in *p*-xylene at	
		80°	100°		80°	100°
Toluene	3.7	9.1	12.6	1.4	3.0	3.3
Methylcyclohexane	3.1	5.5	8.2	1.1	1.6	2.4
Iso-octane	0.5	2.7	5.9	0.6	1.0	1.6

Numerical values of diffusion coefficients are listed in Table 1. Michaels and coworkers[28] ascribe the discrepancy between diffusion coefficients determined by different methods to the fact that in absorption and desorption the diffusion coefficient depends on time as well as on concentration.

Fels[36] reported some measurements of the diffusion coefficient of hydrocarbons in polyethylene by experiments on the absorption of vapours at different activity.

During the diffusional permeation of a multicomponent mixture through a membrane, resulting in separation of the mixture, we cannot assume that the components of the mixture diffuse independently of each other (in parallel flows, as it were). Intermolecular interaction, which is present in the original solution, is undoubtedly complicated by the interaction between the components of the mixture and the membrane material (i.e. the polymer[25,26,42,43,36,53,54]). The diffusion coefficients will depend not only on the concentration of each substance diffusing through the membrane, but also on their physicochemical interactions with each other and with the polymer. This interaction will undoubtedly influence also the concentration profile of the various components across the membrane[37].

Fels and Huang[25,26] suggest two basic reasons for the deviation from additive (i.e. ideal) behaviour of the rate of permeation of a benzene–n-hexane mixture: liquid–liquid interaction, and the plasticising effect of the solutes on the polymer (the presence of a second liquid component in the polymer alters the activity and hence the plasticising effect of the first). A similar view is put forward by Krewinghaus[41], who studied the separation of a benzene–cyclohexane mixture by permeation through modified polyethylene membranes: he treats benzene as a "stronger plasticiser" than cyclohexane.

No information on the diffusion coefficients which apply to the permeation of binary or multicomponent mixtures through a membrane is available in the literature.

4. Desorption from the Lower Surface of the Membrane and Transport from the Desorption Layer to the Gas (or Vapour) Phase

These two stages of the permeation process cannot easily be separated on the basis of published work, and we shall consider them jointly.

Substances which have permeated through the membrane are desorbed from the lower surface, forming a layer of liquid. In principle, however, we could choose experimental conditions such that no liquid is formed on the lower surface of the membrane, and the permeating substances are immediately removed as vapours (for example, by suitably evacuating or heating the space below the membrane). These are exactly the conditions which are most often chosen in practice. Permeation through a membrane can take place at a useful rate also if evaporation from the lower surface is hindered, e.g. if the lower space is maintained at atmospheric pressure or at low temperature: in this case the desorbed liquid simply drains off the lower surface of the membrane [53, 37, 55, 56].

In order to clarify the role of stages 4 and 5 in the separation process, we shall write Fick's second law equation in the form

$$G = -D_c \frac{c_2 - c_1}{l} . \qquad (14)$$

We shall assume that the absorption and desorption processes are fast, and $c_1 = c_S$, but $c_2 = c_g$, where c_g is the equilibrium concentration of the permeating species in the lowest layer of the membrane, corresponding to the concentration of the same species in the vapour. Eqn. (14) becomes

$$G = D_c \frac{c_s - c_g}{l} . \qquad (15)$$

In Eqn. (15) c_S and c_g depend essentially on the temperature, on the composition of the mixture, and on the physicochemical properties of the permeating substances. Furthermore, $c_g = f(p)$, and $p = f(P, t_V)$, where P is the total pressure below the membrane, t_V is the temperature of the vapour, and p is the partial pressure of the permeating substance below the membrane. Hence, $c_g = f(P, t_V)$, and changes in P or in t_V influence p and therefore also c_g. An increase in p produces an increase in c_g, a decrease in the concentration gradient across the membrane, and hence a decrease in the rate of permeation through the membrane, as has been observed experimentally [37, 53, 55, 56]. A change in P or in t_V affects not only the rate, but also the selectivity of the separation. For example, the separation coefficient of a mixture, defined as

$$\alpha = \frac{Y_A}{Y_B} \Big/ \frac{X_A}{X_B} \qquad (16)$$

(where $Y_A(Y_B)$ is the concentration of component A(B) in the mixture permeating through the membrane, $X_A(X_B)$ is the concentration of the same component in the original mixture), can be varied from 1.68 to 1.17 simply by varying P and t_V at constant liquid temperature [53, 56] in the case of the two close-boiling hydrocarbons n-heptane and iso-octane (50 : 50% mixture). Similar results were reported by other workers [57].

The effect of vapour pressure on the rate of permeation and on the selectivity of the separation of toluene–isobutanol mixtures [37] is illustrated in Fig. 3. (the special features of the separation of hydrocarbon–alcohol mixtures are discussed below.)

At P = 760 mmHg it is possible to increase p (by heating the space below the membrane) to such an extent that the rate of permeation almost vanishes. Conversely, by cooling the space below the membrane (still keeping P = 760 mmHg) we can lower p and therefore also c_g, and in this way the rate of permeation can be made comparable to the rate obtained in a fairly good vacuum (of the order of 10 mmHg) [37, 53, 55]. Unambiguous experimental confirmation of the sensitive dependence of the rate of permeation on vapour pressure [57] and on total pressure and vapour temperature [55, 56, 58] has been given in the literature.

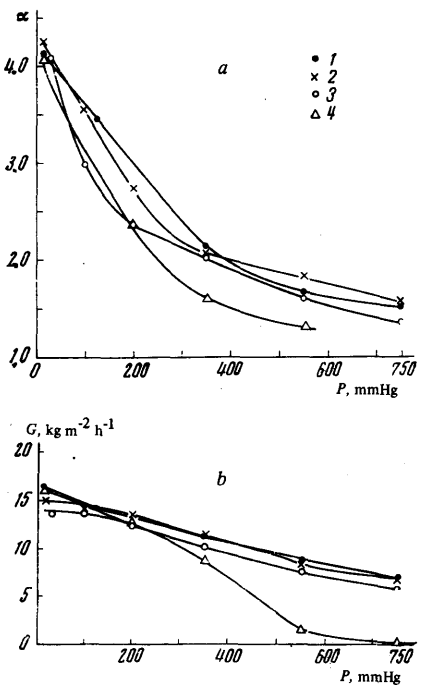


Figure 3. (*a*) Rate of permeation of a 50 : 50% toluene–isobutanol mixture against vapour pressure [37]. Temperature t_T of the heater jacket for the vapour space below the membrane: *1*) 15, *2*) 30, *3*) 50, *4*) 80°; temperature of the liquid 79°. (*b*) Separation coefficient of a 50 : 50% toluene–isobutanol mixture against vapour pressure [37]. Conditions as for Fig. 3*a*.

Ghosh and Rawat [57] have shown that an increase in vapour pressure from 20 to 160 mmHg results in a sharp fall in selectivity of the separation of n-heptane–iso-octane, benzene–cyclohexane, toluene–iso-octane, toluene–methylcyclohexane, and toluene–n-heptane mixtures. In the last three of these mixtures they observed an inversion of the separation: under different conditions the mixture permeating through the membrane may be

enriched in one or the other component. Inversion of the separation of benzene and n-hexane has also been reported [55,58].

Generalising our consideration of the five-stage mechanism of permeation of liquids through polymer membranes, we must stress the need to make proper allowance for each of the stages. Failure to do so may result in serious errors, lack of reproducibility, and incorrect design of apparatus for large-scale operation.

III. INFLUENCE OF POLYMER STRUCTURE AND POSSIBLE MODIFICATIONS OF THE MEMBRANE

Since polyethylene and polypropylene membranes are used almost exclusively at present for the separation of organic liquids by diffusional permeation, we shall not consider other types of membrane in this review.

Several workers have shown [59-63] that in crystalline polymers (such as polyethylene and polypropylene) diffusion is confined almost entirely to the amorphous regions. The permeability of crystalline regions towards gases (He, CH_4) is 2–3 orders of magnitude lower than the permeability of amorphous regions.

Increasing the degree of crystallinity leads to a drastic lowering of the rate of permeation of liquids through the membrane [31,53,64,65], since the permeation of liquids also takes place in the amorphous regions to a large extent. Since dissolution also is largely confined to the amorphous regions, and the diffusion coefficient varies exponentially with the concentration of the liquid in the polymer, decreasing the proportion of amorphous material causes a sharp decrease in the diffusion coefficient.

In a crystalline polymer the amorphous regions are separated by crystalline regions, which thus limit the volume fraction of the polymer available for diffusional permeation. Diffusion takes place along irregular, tortuous channels. Some of the amorphous regions may be close-ended, and not available for continuous permeation. There may also be very narrow channels, which are blocked by the diffusing material.

Not only does the presence of crystalline regions create geometric barriers and lower the rate of permeation, but (even more important) these barriers affect different substances to different extents, as shown by the different rates of permeation of chemically similar but structurally different substances. For example, the rate of permeation of normal alkanes decreases with increasing chain length [1,43,53,55]; iso-alkanes permeate more slowly than normal alkanes [1,43,53]; the xylene isomers [28,31], and benzene and cyclohexane [41,53,54,56], permeate at different rates.

In their paper on the separation of the xylene isomers [31] Michaels and coworkers treat polyethylene as a special type of molecular sieve, in which the intercrystalline pores are filled with amorphous material. On this basis they were able to explain the effect of a "conditioning" treatment on the polymer (lengthy immersion of the membrane in one of the xylene isomers at 50–60° (low-pressure polyethylene) or 90–100° (high pressure polyethylene)). They suggest that during the heat treatment of the membrane the crystals are rearranged without significant change in the degree of crystallinity (for temperatures up to 100°). A more ordered structure, with larger crystals, is formed, the molecules of the xylene isomer acting as "templates" for the reconstruction of the crystalline regions. After this conditioning treatment, the rate of permeation and the selectivity of the separation of the xylene isomer used as a template are significantly increased.

Michaels and Hausslein [46] explain the difference in the sorption capacity for *p*-xylene of polyethylene membranes prepared in different ways by distinguishing between elastically effective and elastically ineffective parts of the amorphous regions. In this model the activity coefficient of the compound dissolved in the polymer is given by the Flory–Renner equation

$$\ln a_p = \ln V_p + (1 - V_p) + \chi(1 - V_p)^2 + \frac{\langle\alpha\rangle_0^2 f \rho V_p (1 - V_p)^{1/3}}{M_c} \qquad (17)$$

rather than by the Flory–Huggins equation (1). In Eqn. (17) $\langle\alpha\rangle_0$ is a geometric factor, taken [46] to be unity, f is the weight fraction of elastically effective polymer, ρ is the density of the unswelled polymer, and M_C is the average molecular weight of the elastically effective regions.

The term elastically effective refers to polymer chains firmly attached to both ends to a cross-linked or to a crystalline region. Polymer chains fixed at one end only, short molecules, and tangles of loose polymer chains are non-elastic. The authors prepared polyethylene membranes with different degrees of crystallinity and different amounts of elastically effective polymer by cooling the membranes from 160° at different rates to 50° (in a dry ice–acetone mixture, in a few minutes, or over a period of 4 hours). Some membranes were mechanically stretched at 40°. The higher cooling rates gave larger amounts of elastically effective polymer. Heat treatment at 130° of samples previously cooled in dry ice–acetone mixture lowered the proportion of elastically effective polymer. Stretching at 40° gave the highest proportion ($f = 0.88$ g g^{-1}) of elastically effective amorphous polymer.

Elastically effective and elastically ineffective regions behave quite differently during dissolution and diffusion. The diffusing molecule can easily draw apart the ineffective, loose regions of the polymer, but it experiences considerable resistance to migration in the regions where the polymer molecules are anchored and elastically effective. As a result, the solubility of the permeating substance in the membrane and its diffusion coefficient are both lowered, but the effect on the diffusion coefficient is much greater than the solubility effect. This is because the diffusion coefficient is an exponential function of the concentration of diffusant in the polymer. For example, the solubility of hydrocarbon vapours in membranes which have been stretched at low temperatures is decreased 2–3 fold, whereas the diffusion coefficient is decreased by a factor of 10–1000.

In a more recent paper, Michaels and coworkers [28] apply the concept of an elastically effective polymer to the conditioning effect on polypropylene membranes of different solvents (methylcyclohexane, *p*-xylene, *o*-xylene, iso-octane, toluene) at temperatures between 60 and 100°. They re-examine their earlier model of the conditioning effect, in which the solvent molecules act as "templates" for the reorganisation of the crystalline regions [31,66], and they show experimentally, for example, that the rate of permeation of iso-octane is substantially increased (4-fold) after treating the membrane in a solvent composed of much smaller molecules (toluene). They also show that the smaller the difference between the Hildebrand solubility parameters of the polymer (polypropylene) and the solute, the lower is the temperature at which the polymer will dissolve. Solvent treatment is thought to involve 2 processes: 1) partial melting of the crystalline regions in the polypropylene and 2) recrystallisation to

give larger crystals. In the resulting structure the amorphous regions are less intimately constrained, less crowded by the crystalline regions, and therefore the proportion of elastically effective polymer is decreased and the diffusion coefficient and rate of permeation are increased. However, the selectivity of the separation is found to vary in inverse proportion to the rate of permeation‡, in contrast to earlier findings [31,66].

A preliminary comparison of polyethylene and polypropylene membranes [28,67] indicates that the diffusion coefficient and the rate of permeation are somewhat higher in the latter. Since the solubility in the two polymers is practically the same, it is concluded that more direct "paths" are available for molecular migration in polypropylene. The greater selectivity of polypropylene towards the separation of xylene isomers is ascribed to greater stiffness of the chains, lower mobility of polymer segments, and greater sensitivity to the size and shape of the permeating molecules in polypropylene.

We must stress that comparisons between polyethylene and polypropylene membranes are arbitrary to a large extent, because both the rate of permeation and the selectivity of the separation are extremely sensitive to the degree of crystallinity and other parameters of the polymer.

Michaels and coworkers [68] have discussed the possible advantages of thermal modification of the membranes; they have also considered modification by mechanical treatment (including unidirectional stretching at low temperatures) [41,69-71] and by solvent treatment [72,73].

They have shown that unidirectional cold stretching (at a temperature well below the melting point) produces drastic changes in the properties of the membrane [41,70,71]. The degree of crystallinity hardly changes at all, but the solubility of the permeating compounds is significantly decreased, the diffusion coefficient falls sharply, so does the rate of permeation through the membrane, and the selectivity of the process is increased. An annealing treatment after unidirectional cold stretching practically restores the original rate of permeation, but at some cost in selectivity (which remains, nevertheless, higher than the selectivity of the original, non-oriented membrane).

These observations are explained as follows. Low-temperature unidirectional stress extends the polymer chains, producing narrow, compressed amorphous channels. The "mobility" of the polymer decreases, and additional barriers to molecular migration in the polymer are produced, leading to a sharp decrease in the rate of permeation. At the same time, the significance of the size and shape of the migrating molecules becomes even more important, and therefore the selectivity of the separation is improved. For example, unidirectional cold stretching of polyethylene membranes at 35° increases the separation coefficient (see Eqn. (16)) of a 50 : 50% mixture of benzene and cyclohexane from ~2 to 4, but the rate of permeation is reduced approximately 30-fold [41].

Krewinghaus [41] therefore confirms the previous suggestion, based on experimental observations [46], that unidirectional cold stretching produces a marked increase in the proportion of elastically effective polymer, and hence a very marked decrease in the diffusion coefficient.

One way of increasing the throughput of this method of separation is to work at higher temperatures: this raises the problem of the thermal stability of the membranes. The thermal stability can be increased, for example, by inducing cross-linking in polyethylene with various forms of ionising radiation [74]. High-pressure polyethylene membranes modified by u.v. irradiation in the presence of PCl_3 have been examined: the rate of permeation of toluene through membranes cross-linked by this technique was found to have risen to 40–60 kg m^{-2} h^{-1}, and the rate of permeation of toluene mixed with ~50% of alcohols had risen to 20–30 kg m^{-2} h^{-1}, without serious loss of selectivity [81]. Cross-linked polyethylene membranes can be used at 80–100°, and in some cases up to 120°, whereas the original membranes were rapidly degraded at 60–65°.

Siegel and Coughlin [75,76] subjected to γ-ray irradiation polyethylene membranes which had been previously immersed in a solvent (benzene, toluene, cyclohexane) for 48 h. The rate of permeation through a membrane modified in this way is increased by about a factor of 2. The authors consider that solvent treatment assists the growth of large crystals at the expense of the smaller crystals, giving rise to a more "open" structure and increasing the number of "amorphous holes". During the subsequent irradiation, the interaction of free radicals in the amorphous regions of the polyethylene results in cementation (or fixation) of a modified structure at the boundaries of the crystalline regions. It is suggested that this method of membrane modification should increase the selectivity of the membrane towards the solvent used for the initial swelling, but the suggestion has not yet been tested experimentally.

Rogers [77] was among the first to study the permeation of gases and vapours (N_2, CO_2, CH_3Br, n-hexane, benzene, methanol) through membranes modified by radiation-induced cross-linking of acrylonitrile, styrene, and vinyl acetate previously sorbed from a solution onto polyethylene.

Huang and Fels [78,79] used γ-radiation to graft styrene from methanol solution onto polyethylene membranes at 35°. The extent of grafting obtained was 5.16 and 26%. They found that as the amount of graft copolymer is increased from 0 to 26%, the coefficient D_0 (see Eqn. (2)) at 45° decreases from 4.49 to 0.90×10^{-8} cm^2 s^{-1} (for the permeation of n-hexane) and from 6.90 to 1.00×10^{-8} (for the permeation of benzene). The solubility of n-hexane is almost unaffected (from 0.228 to 0.245 cm^3 cm^{-3}), but the solubility of benzene is significantly increased (from 0.234 to 0.340 cm^3 cm^{-3} of dry polymer). The authors also studied the changes in free volume $f(V_p, T)$ (see Eqn. (9)), and found that in the polymer–n-hexane system this parameter decreases from 55 to 8% at 45° as the degree of copolymerisation is increased from 0 to 26%. Under similar condition, $f(V_p, T)$ for the benzene–polymer system decreases from 36 to 21%. The activation energies for the permeation of benzene–n-hexane and toluene–n-heptane mixtures through grafted membranes were calculated from the $G-T$ relationships. Increasing the amount of graft copolymerisation lowers the activation energy, and hence increases the rate of permeation (by a factor of 2–3). The observed increase in the separation coefficient α for benzene–n-hexane and toluene–n-heptane mixtures is explained by the lower mobility of the polymer chains after grafting, and by the increased importance of the geometrical parameters of the permeating molecules. The separation coefficient was increased, depending on the extent of graft copolymerisation, by 10–25%.

‡The selectivity of the separation of *p*- and *o*-xylene was defined [28] in terms of the ratio of the rates of permeation of the two isomers.

IV. DEPENDENCE OF THE RATE AND SELECTIVITY OF THE SEPARATION ON THE COMPOSITION OF THE MIXTURE

The rate of permeation through a membrane can be unequivocally calculated from the known rates of permeation and the composition of the mixture to be separated only in a few special ("ideal") cases, such as the separation of mixtures of alkane hydrocarbons[42,53]. In mixtures of hydrocarbons of different classes the rate of permeation is greater than the value expected from the rates of permeation of the individual components and the composition of the mixture. It is given by the equation

$$G_{AB} = G_A X_A \gamma_A + G_B X_B \gamma_B. \qquad (18)$$

where G_{AB} is the rate of permeation of the mixture, γ_A and γ_B are coefficients describing the deviations from additivity (or ideality) for the components A and B, defined as

$$\gamma_A = G_A^v / G_A X_A; \quad \gamma_B = G_B^v / G_B X_B$$

where G_A^p is the partial rate of permeation of the component A for the composition of the mixture and G_B^p is the same quantity for component B.

For an "ideal" mixture of alkane hydrocarbons $\gamma = 1$; for a benzene–n-hexane mixture the value of γ for benzene can be as high as 2.3 [48] or 1.8.[42,53]

As already pointed out, we cannot treat the permeation of the components as a case of parallel flows. The solubility in the membrane of the substances to be separated is affected by the intermolecular interactions of the liquids with each other and with the membrane material. The diffusion coefficients depend not only on the concentrations of all the species present in the membrane, but also on their physicochemical interactions within the polymer structure. The desorption process also is complicated by intermolecular forces. For these reasons, the mathematical description of the permeation of a complex mixture through a membrane is a very difficult problem, which can only be solved at present for a few of the simplest and most fully characterised systems.

Fels and Huang[25,26] attempted a theoretical interpretation of the effect of composition on the rate of permeation of a mixture, allowing for liquid–liquid interactions and for the plasticising effect of the solute molecules on the polymer structure. Starting from the exponential dependence of the diffusion coefficient on concentration, and from Fujita's free volume theory[52], they obtained equations for the rate of permeation of mixtures with different compositions. The required numerical values of $Dc = 0$, $f(0, T)$, $\beta(T)$, and Bd (see Eqn. (10)) were obtained experimentally for the benzene–n-hexane–polyethylene system by desorption experiments described in another paper[50]. The ratio between experimentally observed and calculated rates of permeation is 0.68–2.69 at 25° and 0.93–1.35 at 45°, depending on the initial composition. Fels and Huang ascribe the fairly large discrepancy between experiment and theory to the following effects: 1) inadequacy of the "free volume" concept, 2) the assumption that the concentration c_1 in the upper layer of the membrane has the equilibrium value c_S, 3) the unsupported assumption of a constant concentration ratio of benzene and n-hexane at any point in the membrane, 4) liquid–liquid interaction and liquid–polymer interaction.

Fels[36] points out that his earlier calculations[25,26] involved an elaborate mathematic programme and extravagant use of computer time. He developed a simpler method of calculating rates of permeation of mixtures from the composition of the mixture, the rate of permeation of the individual components, the diffusion coefficient, and the calculated free volume. The diffusion coefficient is determined from the absorption of vapours at different activities, using an equation proposed by Crank[35]:

$$1 - \frac{Q_t}{Q_\infty} = \frac{8}{\pi^2} \exp \frac{D\pi^2 t}{l^2} \qquad (19)$$

where Q_t is the amount of vapour absorbed in time t, and Q_∞ is the total amount of vapour absorbed when equilibrium has been established.

Table 2. Calculated and experimental rates of permeation of cyclohexane and n-heptane through a polyethylene membrane[36].

Temp., °C	Ratio of experimental to calculated rate of permeation for different amounts of cyclohexane in the mixture, wt.%							
	80		60		40		25	
	cyclo-hexane	n-heptane	cyclo-hexane	n-heptane	cyclo-hexane	n-heptane	cyclo-hexane	n-heptane
25	1.27	1.62	1.15	1.36	0.88	1.32	0.86	0.85
30	1.07	1.65	0.99	1.33	0.80	1.27	0.75	0.80

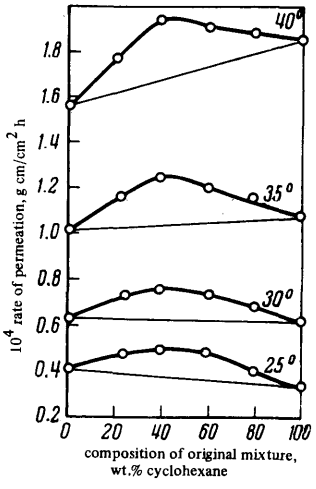


Figure 4. Rate of permeation of a cyclohexane–n-heptane mixture against composition of original mixture[36].

The ratios of experimental to calculated partial rates of permeation for cyclohexane–n-heptane mixtures of different composition are shown in Table 2. Fig. 4 shows experimental plots of the rate of permeation of a cyclohexane–n-heptane mixture as a function of composition.

This mixture does not deviate very strongly from "ideal" behaviour (indicated by the straight line joining the rates of permeation of the pure components). Hence, the results given in Table 2 are unacceptable. Nevertheless, the combined experimental and computational method proposed by Fels[36] has a great deal of merit, because it retains the strictly scientific and logical approach of the earlier attempt[25,26] to describe mathematically the separation of liquids by diffusional permeation through a membrane.

Krewinghaus[41] has tried to evaluate the combined plasticising effect of benzene and cyclohexane on polyethylene. He concludes that benzene is the "stronger" plasticiser, and he gives an empirical equation for the rate of permeation of a mixture with allowance for composition and for the plasticising effects of benzene and cyclohexane.

Several workers have reported (without comment) composition effects on the rate of permeation and selectivity during the separation of toluene–n-butanol mixtures (polypropylene membrane)[21,23] and benzene–isopropanol and benzene–methanol mixtures (polyethylene membrane)[32]. We should point out that whereas the separation coefficient α is usually less than 2 for mixtures of hydrocarbons (for example, benzene–n-hexane, n-heptane–iso-octane, benzene–cyclohexane, mixtures of xylene isomers, etc.), in mixtures of hydrocarbons and polar compounds (alcohols, acetic acid[23]) the separation coefficient is much higher (10–25, or even higher).

V. INFLUENCE OF THE NATURE OF THE COMPOUNDS TO BE SEPARATED

Although the influence of the nature of the compounds to be separated has been implicit in the whole of the preceding discussion, the subject is so important that we think it right to devote a special Section to it. It is the most complicated and the least clearly understood of all the problems which arise in the study of permeation. The difficulty stems from the fact that the permeation process takes place in several stages, and we must therefore consider a wide range of properties of the permeating liquids and of the polymer: boiling point, solubility in the other components of the liquid mixture and in the polymer, polarity, structure and size of the molecules, heat of evaporation, etc.

By analysing published data obtained under conditions such that $c_2 = 0$ and the resistance of steps 4 and 5 can be ignored, we can draw a number of general conclusions on the expected order of separation: 1) the lower members of a homologous series permeate faster than the higher members, 2) if two molecules have the same molecular weight and similar chemical nature, the one with the smaller cross-sectional area permeates faster, 3) if the only difference between the components is the degree of unsaturation, the more unsaturated species permeate faster, 4) the molecules which permeate fastest are those least likely to form hydrogen bonds with the material of the membrane.

The fourth conclusion is illustrated by the following example. The separation of chloroform–acetone mixtures with Teflon membranes is ascribed[80] to the fact that chloroform has an active hydrogen atom, and the fluorine atoms in Teflon have donor properties: as a result, hydrogen bonds are formed and the chloroform is held relatively firmly by the Teflon. In practice only acetone permeates through the membrane, and the chloroform is completely retained.

Most of the work on the separation of organic liquids by diffusional permeation through membranes has been done with hydrocarbons, whose rates of permeation through a given membrane are not very different. However, the separation of hydrocarbons from polar compounds (in particular, alcohols) is also a problem of great practical importance. Using the conventional polyethylene and polypropylene membranes, we would expect the rates of permeation of the hydrocarbon to be 2 orders of magnitude greater than the rate of permeation of the alcohol, leading to a very efficient separation of these mixtures. This expectation is not always borne out by experiment.

El'bert and coworkers[37] have suggested that the properties of the slowly permeating component are not the only factor (or even the main factor) determining the partial rate of permeation of the slow component (alcohol) when mixed with a fast permeating component (hydrocarbon) Hence, the properties of the slow component are not the only factor determining the selectivity of the separation. The solubility and the diffusion coefficient of the slow component are determined not only by the properties of this component and those of the polymer, but first and foremost by the concentration of the faster component at each point in the membrane and by its plasticising effect on the membrane. The fast diffusing substance, being dissolved in the membrane, appears to retain its power to dissolve the slowly diffusing substance, and is able to "drag" it across the membrane.

The same paper[37] describes an experimental study of the separation of a toluene–isobutanol mixture by permeation through polyethylene membranes modified by photochemical cross-linking. On cooling the space below the membrane, and raising the pressure from 20 to 760 mmHg, the selectivity of the separation is found to decrease very substantially. The following explanation is proposed: toluene is readily soluble in the polymer (according to Long, the solubility of toluene in polypropylene is 0.23 g g^{-1} of dry polymer at 60° [29]). Hence, the upper layer of the membrane, where the concentration is close to the equilibrium value, becomes essentially a gel with a high percentage of toluene, and the alcohol is dissolved by this gel rather than by the membrane material. On evacuating the space below the membrane (to a pressure of 10 to 20 mmHg) the concentration of toluene decreases sharply over the entire thickness of the membrane, and practically vanishes in the lower layer of the membrane[38]. In such a membrane (with a "damp" top layer and a "dry" bottom layer) the slowly migrating component has to pass from a region of extensively plasticised polymer, with a high concentration of fast diffusing solute, to a region where practically no plasticising has taken place. Thus, the geometrical barriers opposing migration of the alcohol increase throughout the thickness of the membrane. As a result, the partial rate of permeation of the alcohol is small, and the separation coefficients is acceptably high.

It is also pointed out[37] that on increasing the pressure below the membrane to 760 mmHg and cooling the space below the membrane the concentration profile across the membrane is greatly altered, and the concentration of the fast diffusing substance (toluene) is so high over the entire thickness of the membrane that the slowly diffusing substance (alcohol) is able to migrate across the membrane, which is now a gel (with a high concentration of plasticiser) over its entire thickness. In a "damp" membrane of this kind the geometrical barriers to migration of the alcohol are much lower than in a "dry" membrane.

As a result the separation coefficient of the toluene–isobutanol (50 : 50 wt.%) mixture decreases from 4.5 (at 15 mmHg) to 1.6 (at 760 mmHg).

The plasticising effect of hydrocarbons can be so marked that a hydrocarbon–alcohol mixture permeating through the membrane becomes enriched in the alcohol, although its individual rate of permeation through the membrane is 2 orders of magnitude lower [82].

Thus, a knowledge of the physicochemical properties of the compounds to be separated is far from sufficient to identify the order of the separation. We must also consider the way in which liquid–liquid and liquid–polymer interactions respond to changes in the experimental conditions, and first and foremost we must consider the temperature of the liquid and the temperature and pressure of the vapour.

VI. INFLUENCE OF TEMPERATURE OF THE LIQUID

As a rule, the rate of permeation through a membrane increases exponentially with the temperature of the liquid [17,21,23,28,53,56]. Michaels and coworkers [28] suggest 3 main reasons for the steep increase in rate of permeation: 1) activation of the molecules by the increase in temperature, 2) increased activity of the diffusing species in the polymer resulting from the lower compression, extension, etc. of the polymer chains in the amorphous phase (some decrease in the content of elastically effective polymer is also possible—this point is also stressed by Hausslein [83]), 3) the solubility of the permeating species in the polymer increases with temperature, and the diffusion coefficient is an exponential function of concentration.

The activation energy of the process of permeation through a membrane is usually in the range 7 to 10 kcal mole^{-1}.

Increase in the temperature of the liquid usually produces, in addition to a large increase in the rate of permeation, also a significant decrease in selectivity [17,21,31,28,37,42,56,69]. Michaels and coworkers [28] ascribe this effect to a decrease in the stiffness of the amorphous phase resulting from the combined solvent and temperature effects on the polymer: the polymer is plasticised, and the influence of geometrical barriers on the migration of molecules through the membrane becomes less marked.

Dytnerskii and Golovin [21] have shown, in the special case of the separation of an azeotropic mixture of toluene and n-butanol (containing 72 vol.% of toluene), that a reversible dependence of permeation rate on temperature is observed only if the polypropylene membrane is previously heated to the highest temperature in the experimental range.

Similar results were later reported by Michaels and coworkers [28], who consider that experiments at high temperature have an irreversible effect on the structure of the polymer by lowering the proportion of elastically effective polymer and partly releasing the internal stresses in the amorphous phase. It is pointed out that an increased rate of permeation of a given substance through a membrane can be obtained by previously subjecting the membrane to a high-temperature treatment in a solvent which does not need to be the same as the experimental liquid. For example, treatment of a polypropylene membrane at 60° in iso-octane, toluene, n-hexane, *p*-xylene, and methylcyclohexane increases the rate of permeation of iso-octane at 40° by factors of 2.07, 4.1, 3.58, 2.28, and 5.78 respectively. The selectivity of the separation is found to be somewhat lower after this treatment, in contrast to an earlier report [21] that the selectivity is unaffected.

Li and Long [84] measured the temperature dependence of the rate of permeation of a series of aromatic and non-aromatic hydrocarbons, acetic acid, methanol, water, ethyl methyl ketone, carbon tetrachloride, pyridine, and ethanol through polypropylene membranes. They also measured the effect of temperature on the permeation through Teflon membranes of n-heptane, toluene, ethanol, water, and on the permeation through Saran membranes of toluene, n-heptane, and ethanol. They found that when the permeation of non-aromatic hydrocarbons through polypropylene membranes at temperature in the range 10–70° is plotted as $1/T$ against $\ln G$ the curve shows a break at temperatures between 20 and 45°, corresponding to a sudden change in slope, and therefore also to a change in the activation energy of the permeation process. The break is not found in plots of the permeation of aromatic hydrocarbons through polypropylene membranes.

Chartov and coworkers [81] have shown that the rate of permeation of *o*-xylene and of a toluene–isobutanol (50 : 50%) mixture through photochemically modified polyethylene membranes is not an exponential function of temperature. The rate of permeation was measured at temperatures between 60 and 100° (for the toluene–isobutanol mixture) and between 60 and 120° (for *o*-xylene). The deviation from exponential behaviour is explained as follows: during photochemical cross-linking the new bonds are formed preferentially in the amorphous regions [85]. However, under the influence of a solvent and of elevated temperature we can expect partial dissolution of the crystalline regions, with formation of amorphous regions which are not cross-linked. Since the molecules diffuse through the amorphous regions of polyethylene, this process widens the permeation front, and furthermore the rate of permeation is different in the amorphous regions with and without cross-linking.

As already pointed out, an increase in temperature leads to an increased rate of permeation through the membrane, and at the same time it lowers the selectivity of the separation process. Hence, an optimum choice of temperature is most important since it allows the total area of the membrane to be decreased in industrial processes. It is stated [28] that the number of separation stages required to achieve a given degree of enrichment of one of the components is approximately inversely proportional to the logarithm of the separation coefficient (i.e. $\lg \alpha$), and the separation surface at each stage is inversely proportional to the rate of permeation (by raising the temperature), though accompanied by some loss of selectivity, could result in a decrease of the total working surface of the membrane required for an industrial apparatus. However, if $\alpha \simeq 1$ a small loss of selectivity, even if accompanied by a large increase in the rate of permeation, could greatly increase the number of separation stages required, and thus increase the total membrane area.

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The selectivity of separation methods based on diffusional permeation through polymer membranes is determined by a set of properties entirely different from those relevant to other methods of separation currently used in industry (fractionation, absorption, adsorption, crystallisation). Hence this method of separation could successfully be adopted industrially for the following operations:

1) separating mixtures of compounds of similar chemical nature and having similar boiling points (e.g. benzene and cyclohexane); 2) separating mixtures of isomers (for example, xylene isomers, normal and iso-alkanes); 3) separating various azeotropic mixtures (for example, mixtures of toluene and isobutanol, which form an azeotrope and boil at 110.6 and 108° respectively under atmospheric pressure).

Many different practical designs, and technological variants of the process, have been described. For example, "evaporation through a membrane" and "extraction through a membrane"[10], in which the substances migrating across the membranes are removed in a stream of air (or water vapour) or in a flow of inert solvent. Michaels and Bixler[10] point out that membranes suitable for use in the chemical and petrochemicals industry already exist. The main obstacle to the penetration of this method of separation into industrial practice is the unconventional design and operating mode of the necessary plant, which is radically different from traditional separation plant and therefore needs to be specially developed for the purpose.

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Zelinskii Institute of Organic Chemistry
of the USSR Academy of Sciences,
Moscow

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Vibration Spectra and Structures of the Simplest Aromatic Derivatives of Group I-VI Elements

A.N.Rodionov

The review gives a general and systematic account of experimental and calculated data on the vibration spectra and structures of the simplest aromatic derivatives of non-transition Group I-VI elements. Particular attention has been devoted to "M-sensitive" vibrations, i.e. vibrations involving the element M, the frequencies of the corresponding bands, their activites, and the splittings of the components as a function of molecular structure. The monosubstituted benzene approximation is shown to have poor suitability for the interpretation of the spectra of derivatives of polyvalent elements. The bibliography includes 145 references

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I. INTRODUCTION

The extremely common occurrence of aromatic compounds in natural and synthetic materials is generally known. The specific features of aromatic molecules associated with the delocalisation of π electrons and the transmission of electronic effects from one part of the molecule to the entire conjugated system have found extremely wide applications in science and engineering. The creation of new materials with specified properties requires a profound study of the various factors which affect the structure and physicochemical characteristics of aromatic molecules. One of the physical methods most widely employed is that of vibration spectroscopy with which it is often possible to determine the structure of the compound, the type and nature of the substituent, the stability and structure of the complexes, etc.

Therefore this method has been widely used in the last 10–20 years in analytical and structural studies on numerous aromatic compounds, particularly in view of its availability to a wide circle of not only spectroscopists but also chemists working on synthesis. Monographs devoted fully or partly to the vibration spectra of aromatic derivatives have been published in recent years both in the USSR and abroad[1-3]. However, the vibration spectra of purely aromatic molecules of different structures are as a rule discussed in these general texts. In those cases where a substituent is introduced into the aromatic system it usually consists of hydrocarbon groups (aliphatic, unsaturated, etc.) or halogen atoms.

There has now been an appreciable growth of interest in heteroaromatic molecules containing heteroatoms of different types. Studies have been made in recent years on the vibration spectra of compounds of this type but so far these have been non-systematic and sometimes contradictory.

The present review attempts to compile and arrange systematically the original studies on the vibration spectra and structures of the simplest aromatic derivatives of Group I–VI elements and to demonstrate the possibility of employing these spectra for the identification of the individual Ar–M bonds, to determine their strength, and to investigate the molecular structure.

A single system of notation for vibrations is at present lacking in the literature on the vibration spectra of the simplest aromatic compounds (monosubstituted benzenes). In the discussion of the vibration spectra of aromatic compounds with hydrocarbon substituents, one usually employs the notation proposed by Herzberg[2] or Wilson[4]. However, in most studies on the vibration spectra of aromatic derivatives of the elements, Whiffen's notation has been used[5]. Since the present review deals with the spectra of compounds of the second type, we shall continue to employ Whiffen's notation for the vibrations of monosubstituted benzenes in order to simplify comparison with the original studies.

The conversion from one system of notation for monosubstituted benzene vibrations to the other is illustrated in Table 1 which includes in addition the vibration symmetries and approximate absorption regions.

Analysis of the experimental and theoretical data on the vibration spectra of many phenyl derivatives of various elements shows the complexity of the majority of vibration modes. Thus, in contrast to aliphatic derivatives of the elements where stretching and deformation vibrations of the C–M bond can be more or less clearly distinguished, in aromatic derivatives there are as a rule several vibrations in which the Ph–M group is involved to different extents.

According to Whiffen's suggestion[5], these vibrations are called "M-sensitive". These vibrations are in fact of greatest interest in the study of the nature of the substituent and molecular structure and therefore they will be henceforth discussed in greatest detail. On the other hand, the vibrations of the benzene ring, which do not involve the heteroatom, will be considered only where they throw light on the structure of molecules or their complexes.

It is noteworthy that, in contrast to phenyl derivatives of univalent Group VII elements, the spectra of which were studied by Whiffen[5], for polyvalent heteroatoms (with several substituents linked to a single heteroatom), one

must take into account the overall molecular symmetry; this may lead to the splitting of the bands owing to the interaction of the vibrations of adjacent groups via the central atom.

Table 1. The notation, symmetry, and absorption regions of the vibrations of monosubstituted benzenes (C_{2v}).

Notation according to Refs.						Notation according to Refs.					
2	4	5	based on vibration modes	Vibration symmetry	Absorption region, cm^{-1}	2	4	5	based on vibration modes	Vibration symmetry	Absorption region, cm^{-1}
1	2	z_1	ν_{C-H}	a_1	3060	13′	19*a*	*n*	ν_{C-C}	e_1	1450
2	1	*r*	ν_{C-X}	a_1	650—800	14	18*a*	*b*	β_{C-H}	a_1	1030
3	3	*e*	β_{C-H}	e_1	1270	14′	18*a*	*u*	β_{C-X}	e_1	200—500
4	11	*f*	γ_{C-H}	e_2	750	15	7*a*	z_5	ν_{C-H}	e_1	3045
5	13	z_2	ν_{C-H}	a_1	3060	15′	7*a*	z_3	ν_{C-H}	a_1	3045
6	12	*p*	α_{CCC}	a_1	1000	16	8*a*	*l*	ν_{C-C}	e_1	1590
7	5	*j*	γ_{C-H}	e_2	982	16′	8*a*	*k*	ν_{C-C}	a_1	1605
8	4	*v*	δ_{C-C}	e_2	697	17	9*a*	*c*	β_{C-H}	e_1	1155
9	14	*o*	ν_{C-C}	e_1	1325	17′	9*a*	*a*	β_{C-H}	a_1	1175
10	15	*d*	β_{C-H}	e_1	1070	18	6*a*	*s*	α_{CCC}	e_1	620
11	10*a*	*g*	γ_{C-H}	a_2	835	18′	6*a*	*t*	α_{CCX}	a_1	250—625
11′	10*a*	*i*	γ_{C-H}	e_2	910	19	17*a*	*h*	γ_{C-H}	a_2	960
12	20*a*	*q*	ν_{C-X}	a_1	1050—1220	19′	17*a*	*y*	γ_{CCX}	e_2	430—500
12′	20*a*	z_4	ν_{C-H}	e_1	3080	20	16*a*	ω	γ_{CC}	a_2	405
13	19*a*	*m*	ν_{C-C}	a_1	1500	20′	16*a*	*x*	γ_{CCX}	e_2	150—250

Table 2.

Type of compound	Symmetry point groups	M-sensitive vibrations active in	
		i.r.spectra	Raman spectra
Ph_2M, $PhMX$, Ph_2MX, $PhMX_2$, Ph_2MX_2	C_{2v}	$A_1+B_1+B_2$	$A_1(p)+B_1(d)+B_2(p)$
Ph_2M, Ph_2MX	C_2	A+B	A(p)+B(d)
Ph_3M, Ph_3MX, $PhMX_3$	C_{3v}	A_1+E	$A_1(p)+E(d)$
Ph_3M	C_3	A+E	A(p)+B(d)
Ph_2M	D_{2h}	$B_{1u}+B_{2u}+B_{3u}$	$A_g(p)+B_{1g}(d)+B_{2g}(d)+B_{3g}(d)$
Ph_2M	D_2	$B_1+B_2+B_3$	$A(p)+B_1(d)+B_2(d)+B_3(d)$
Ph_3M	D_{3h}	E′	$A'_1(p)+E'(d)+E''(d)$
Ph_3M	D_3	A_2+E	$A_1(p)+E(d)$
Ph_4M	Td	F_2	$A_1(p)+E(d)+F_2(d)$
Ph_4M	S_4	A+E	A(p)+B(d)+E(d)

Notation. p = polarised; d = depolarised.

This effect should probably be shown most markedly in vibrations involving the heteroatom, i.e. in M-sensitive vibrations. Depending on molecular symmetry, the components of the split band can appear in different ways in the infrared and Raman spectra. Table 2 gives the selection rules for the infrared and Raman spectra of M-sensitive vibrations corresponding to different molecular symmetries.

II. VIBRATION SPECTRA AND STRUCTURES OF PHENYL DERIVATIVES OF GROUP I ELEMENTS

The structures of aromatic derivatives of Group I elements have been hardly investigated at all. The formation of stable dimers has been demonstrated for the lithium derivatives [6,7]. There is no unanimous view as to the nature and structures of these association complexes. Wittig suggests that the structure of the phenyl-lithium dimer be regarded as that of the autocomplex $(Ph_2Li)^-Li^+$, [6] while in other studies it is believed that a cyclic dimer may exist as a result of "electron-deficient" bonds [7]. An increase of the C–M bond polarity in the series Li → Na → K → Rb, Cs is known to occur in alkali metal compounds and therefore, starting with sodium, the C–M bond is usually regarded as mainly ionic.

Lanpher [8] measured the infrared spectra of phenyl derivatives of lithium, sodium, and potassium and found an intense band in the range 1160–1260 cm^{-1} which he assigned to the C–M bond vibration on the basis of its shift when one metal is replaced by another. However, it has been shown [7,9,10] that the band near 1250 cm^{-1} in the spectra of PhLi does not undergo an isotopic shift on replacement of lithium-7 by lithium-6 and therefore cannot be assigned to the C–Li stretching vibration. The use of compounds containing different proportions of the lithium-7 and lithium-6 isotopes made it possible to isolate in the spectra bands associated with the Ar–Li vibration in the dimers (Table 3).

Table 3. C–Li... absorption bands in the infrared spectra of dimeric lithium aryls (cm^{-1}). [7]

Compound	Medium	
	in liquid paraffin	in butyl ether
[^{7}Li]-Phenyl-lithium	280,320,350,427	352,390,440
[^{6}Li]-Phenyl-lithium	290,326,357,430	no data available
[^{7}Li]-*o*-Tolyl-lithium	327,390,420	345,383,421,432
[^{6}Li]-*o*-Tolyl-lithium	338,400,420	278,354,387,440
[^{7}Li]-*p*-Tolyl-lithium	275,310,353	357,395
[^{6}Li]-*p*-Tolyl-lithium	297,318,362	365,416
[^{7}Li]Mesityl-lithium	278,314,342	—
[^{6}Li]Mesityl-lithium	290,326,357	—
[^{7}Li]-α-Naphthyl-lithium	335,383,407	352,390
[^{6}Li]-α-Naphthyl-lithium	350,390,410	360,410

Comparison of the infrared spectra of the PhLi and monosubstituted benzenes with a substituent of similar mass revealed the absence from the spectra of the former of bands sensitive to the substituent in the region above 700 cm^{-1} [for example the 1220 cm^{-1} (*q*-vibration) and 806 cm^{-1} (*r*-vibration) bands in the infrared spectrum of PhF]. [11] This effect is observed in the spectra of all the aromatic lithium derivatives investigated and can probably be accounted for by a weakening of the C–Li bonds owing to stable association of the electron-deficient type. Calculations on in-plane vibrations for the monomeric model of PhLi indeed showed that, even without taking into account the change in molecular configuration on dimerisation, when the force constant K_{Ph-Li} decreases to 1.5×10^6 cm^{-2} the bands in the regions expected for *q*- and *r*-vibrations cease to shift on isotopic substitution of lithium-7 by lithium-6 [12] and, in agreement with experimental data, the isotopic shift occurs only in the long-wavelength part of the spectrum (374 and 259 cm^{-1} for lithium-7 and 400 and 270 cm^{-1} for lithium-6). Moreover, it is noteworthy that the infrared spectra of all the lithium aryls investigated show additional bands in the C–H stretching region displaced towards longer wavelengths by 50–100 cm^{-1}

together with bands in the normal ν_{C-H} region (3030 to 3100 cm^{-1}). The decrease of the ν_{C-H} band intensity in the infrared spectra of lithium aryls is probably associated with a weakening of the C–H bonds in the *ortho*-position relative to the C–Li group, which is satisfactorily correlated with the effect observed in the ^1H NMR spectra of PhLi (Ladd [13]) and is consistent with the decrease in the frequency of the α-C–H bonds in the infrared spectra of aliphatic organolithium compounds [14,15].

III. VIBRATION SPECTRA AND STRUCTURES OF PHENYL DERIVATIVES OF GROUP II ELEMENTS

The presence of vacant p-orbitals and the relatively low electronegativity of beryllium and magnesium result in a fairly stable association of organic derivatives of these elements. The structures of the association complexes of $(CH_3)_2Be$ and $(CH_3)_2Mg$ have been investigated and an appreciable departure of the molecular framework from linearity has been noted ($\angle CBeC \simeq 114°$; $\angle CMgC \simeq 105°$). [16]

Table 4. Experimental and calculated frequencies (wave-numbers, cm^{-1}) of the M-sensitive vibrations in the spectra of Ph_2Be and Ph_2Mg (Rodionov et al. [18]).

Designation of vibration according to Whiffen (Ref.5)	Symmetry (C_2)	Ph_2Be		Ph_2Mg	
		i.r. spectra	calc. for $\alpha = 120°$	i.r. spectra	calc. for $\alpha = 120°$
q	B	1250 m.	1265	1045 m.s.	1060
	A	1200 m.	1198		1075
r	B	902 s.	900	670 m.	675
	A	780 m.	800		685
t	B	570 m.	582	425 s.	415
	A	545 m.	540	310 s.	358
		250 w.	236	200 w.	200
u	B	410 m.	380	255 m.	257
		225 m.	202		185
y	B	475 m.		425 s.	

Note. The following designation of band intensities has been adopted in Tables 4–15: s = strong (intense), m = medium, w = weak, p = polarised, d = depolarised.

We were unable to find direct data concerning the structure of compounds of the type Ph_2M but the fairly large dipole moment of Ph_2Be in benzene [17] and X-ray diffraction data for the crystalline ether adduct of PhMgBr suggest that aromatic derivatives of beryllium and magnesium also have a bent structure with $\angle CMC$ smaller than 180° but probably somewhat larger than for methyl derivatives. In this case structures with C_{2v} or C_2 symmetries are possible. For C_{2v} symmetry, class A_2 vibrations are inactive in the infrared. The decrease of molecular symmetry to C_2 results in all the vibrations becoming active in the infrared and Raman spectra.

We investigated the infrared spectra of Ph_2Be and Ph_2Mg in the range 200–3500 cm^{-1} [18] and assigned the principal bands and confirmed the bent structure of the molecules by comparison of experimental data with the frequencies and vibration modes calculated for different conformations of the Ph_2M molecules.

Table 4 presents bands assigned to the components of the M-sensitive vibrations in the above investigation. In accordance with the selection rules for the proposed molecular symmetry, both components of the M-sensitive vibrations are fairly intense in the infrared spectra, the splitting between them depending significantly on the C–M–C angle. It is noteworthy that, as for PhLi, the association of aromatic derivatives of beryllium and particularly of magnesium leads to a decrease of the force constant K_{C-M} and the appearance in the C–H stretching region in the infrared of C–H bands displaced towards longer wavelengths, in agreement with the ^1H NMR data for PhMgX solutions [13].

The band near 365–383 cm^{-1} in the infrared spectra of ethereal solutions of Ph_2Mg and PhMgBr, assigned by Salinger and Mosher [19] to the stretching PhMg vibration, is probably the B component of the t-vibration with its frequency reduced owing to the formation of an ether adduct.

IV. VIBRATION SPECTRA AND STRUCTURES OF PHENYL DERIVATIVES OF GROUP IIB ELEMENTS

1. Compounds of the Type Ph_2M

Aromatic derivatives of zinc, cadmium, and mercury are monomeric [20–22]. There are X-ray diffraction data demonstrating the linearity of the C–M–C framework of aliphatic derivatives of these elements [23] and also of Ph_2Hg. [24,25] On this basis a planar structure with D_{2h} symmetry has been adopted for Ph_2Zn, Ph_2Cd, and Ph_2Hg, but, as a result of the presence of a centre of symmetry, it should lead to an alternative prohibition: B_u vibrations are active only in the infrared and class Ag and B_g vibrations are active only in the Raman spectra. Unfortunately only the infrared spectra of these compounds have been studied sufficiently fully and the spectra have been interpreted by analogy with monosubstituted benzenes without taking into account the overall molecular symmetry. Therefore the infrared bands assigned [21,26,27] to M-sensitive vibrations should probably be regarded as B_u components of these vibrations active in the infrared spectra. Although the Raman spectra of Ph_2Zn (Kubas and Shriver [28]) and Ph_2Hg (Rodionov et al. [12]) published recently are in fact very incomplete, when combined with calculations on the in-plane vibrations of these molecules [12] they make it possible to detect certain symmetrical components of the M-sensitive vibrations. Table 5 lists the experimental and calculated wave-numbers of the M-sensitive vibrations of diphenyl compounds of zinc, cadmium, and mercury. The results show that the t-vibration, which appears in the range from 200 to 330 cm^{-1} with all the components, shows the maximum splitting of the B_{3u} and Ag components and the greatest sensitivity to the replacement of one metal by another. The 462 and 496 cm^{-1} bands, assigned [29] to the C–Hg–C stretching vibrations in the infrared spectra of $(C_6H_5)_2Hg$ and $(C_6F_5)_2Hg$ respectively, are probably associated with an out-of-plane y-vibration.

The effect of the deuteriation of the benzene rings on the position of the M-sensitive bands in the infrared spectra of $(C_6D_5)_2Zn$ and $(C_6D_5)_2Hg$ has been investigated [21,26]. It has been shown that the B_{3u} components of the t-vibration hardly change on deuteriation, while the r- and q-vibrations shift towards longer wavelengths by 30–40 cm^{-1}; on the other hand, according to Mink et al. [26] the wave-number of the q-vibration of $(C_6D_5)_2Hg$ decreases by approximately 100 cm^{-1}.

2. Compounds of the Type PhMX

X-Ray diffraction data demonstrated the linearity of the C–Hg–Cl and PhHgCl frameworks [30]. The structures of the analogous zinc and cadmium compounds are unknown. If it is assumed that all the compounds discussed in this section have a monomeric linear structure with C_{2v} symmetry, then, in contrast to compounds of the type Ph_2M, only class A_2 vibrations are inactive in the infrared.

Table 5. Experimental and calculated frequencies (wavenumbers, cm^{-1}) of the M-sensitive vibrations in the spectra of Ph_2M (M = Zn, Cd, or Hg).

Vibration		Ph_2Zn			Ph_2Cd		Ph_2Hg		
		expt.					expt.		
Designation	Symmetry (D_{2h})	i.r. spectra according to (Ref.21)	Raman spectra according to (Ref.28)	Calcn. based on Ref.18	i.r. spectra according to (Ref.21)	Calcn. based on Ref.18	i.r. spectra according to (Ref.21)	Raman spectra according to (Ref.18)	Calcn. based on (Ref.18)
q	B_{3u}	1076 s.		1070	1070 m	1065	1075 m.	—	1070
	A_g	—	—	1085	—	1080	—		1080
r	B_{3u}	677 s.		679	672 s.	670	670 s.	—	672
	A_g	—	666 m.	687	—	680	—	670 m.	685
t	B_{3u}	305 s.	—	325	270 s.	280	252 s.	—	253
	A_g	—	210 s(p)	210	—	205	—	212 s(p)	210
u	B_{2u}	220 m.	—	235	—	227	—	—	237
	B_{1g}	202 w.	—	197	—	190	—	—	193
y	B_{1u}; B_{2g}	430 s.		—	445 m	—	452 s.	—	—
		445 s.	455 w.				462 s.	—	—
x	B_{1u}; B_{2g}	170	170	—	—	—			

Table 6. Experimental and calculated frequencies (wavenumbers, cm^{-1}) of the M-sensitive vibrations in the spectra of PhMX (M = Zn, Cd, or Hg; X = Cl, Br, or I).

Designation of vibration according to Whiffen (Ref.5)	Vibration symmetry (C_{2v})	PhZnI (Ref.21)		PhCdI (Ref.21)		PhHgCl(Ref.26)		PhHgBr (Ref.26)		PhHgI (Ref.26)	
		i.r. spectra	calc.	i.r. spectra	calc.	i.r. spectra	calc.	i.r. spectra	calc.	i.r. spectra	calc.
q	A_1	1075	1063	1064	1040	1092	1142	1096	1141	1095	1137
r	A_1	672	660	672	660	674	666	674	664	671	661
t	A_1	280	310	250	250	220	241	216	204	242	247
u	B_1	185	210	—	225	184	223	198	228	213	223
y	B_2	445	470	443	465	453	468	454	468	451	468
x	B_2	165	190	—	162	180	163	175	163	160	163
ν_{M-X}	A_1	230	240	—	165	330	344	257	263	167	174

The infrared spectra of a large number of compounds with the general formula PhHgX, where X = Cl, Br, I, S, OH, O, CO, NO_3, etc. have been described in a review [27]. However, an adequate interpretation of the infrared spectra has been made only for the simplest derivatives PhHgCl, [21,26,27] PhHgBr, PhHgI, [26,27] PhZnI, and PhCdI. [21] The M-sensitive vibrations listed in Table 6 were isolated by analysing the experimental infrared spectra and by calculations on in-plane vibrations.

V. VIBRATION SPECTRA AND STRUCTURES OF PHENYL DERIVATIVES OF GROUP IIIB ELEMENTS

1. Compounds of the Type Ph_3M

It has been established experimentally that Ph_3B, Ph_3Ga, PhIn, and Ph_3Tl are monomeric in solutions and that only Ph_3Al is appreciably associated [20,31]. X-Ray [32] and electron [33] diffraction data indicate a planar trigonal structure of the central MC_3 unit in Ph_3B, Ph_3Ga, and Ph_3In molecules with D_{3h} symmetry and with the symmetry reduced to D_3 for the molecule as a whole owing to the relative positions of the phenyl groups. Ph_3Al crystals contain molecular dimers with symmetrical bridging phenyl groups [34]. These dimers are at least partially retained in solutions [35]. Therefore Ph_3Al presumably has a distorted planar molecular framework and there is probably a transition to C_{3v} or C_3 symmetry. Table 2 shows that the selection rules for the vibration spectra of molecules with D_{3h} and D_3 symmetries indicate that the M-sensitive vibrations (A_1' or A_1) are forbidden in the infrared and are active with marked polarisation in the Raman spectra. Degenerate vibrations (E′ or E) are active both in the infrared and Raman spectra and are depolarised. When the planar skeleton is distorted, i.e. on passing to C_{3v} symmetry, the symmetrical vibrations are no longer forbidden and the class A_1 vibrations should appear in the infrared spectra.

The infrared spectrum of Ph_3B was reported for the first time by Sharp and Sheppard [36] and that of Ph_3Al by Costa and coworkers [37,38], but without a detailed interpretation of the observed frequencies and their assignment. The infrared spectra of crystalline specimens of Ph_3B (Shurvell and Faniran [39,40]) and Ph_3Al (Shurvell [41]) have been measured and the observed bands have been assigned in terms of monosubstituted benzenes (local C_{2v} symmetry).

The present author and his coworkers [31,42,43] investigated the infrared spectra of triphenyl derivatives of boron, aluminium, gallium, and indium from 200 to 3200 cm^{-1} in different states of aggregation. In order to interpret the spectra, specimens enriched in boron-10, boron-11, and deuterium were obtained and calculations were made on the normal vibrations for the Ph–M and C_6D_5–M models. Subsequently the same investigators obtained the Raman spectrum [44] of Ph_3B and carried out calculations for the in-plane molecular vibrations of the class E′, A_1', and A_2' discussed in this section [12,44]; this yielded a complete interpretation of the vibration spectrum and demonstrated unambiguously the planar structure of the BC_3 central unit. Table 7 lists the experimental and calculated wavenumbers of the M-sensitive vibrations of the Ph_3M molecules, where M = B, Al, Ga, or In.

2. Compounds of the Type Ph_2MX

We were unable to find in the literature any direct measurements designed to elucidate structures of this type. Ph_2BCl and Ph_2BBr are known to be monomeric and they have been assigned the C_{2v} or C_2 symmetry with a planar central unit and rings displaced to some extent from this plane. All the vibrations of the C_2 structure are active in the infrared. The analogous aluminium and gallium compounds are dimerised and have M–X...M bridges [45], which leads to a distortion of the plane of the C_2MX central unit. The infrared spectra of compounds of the type Ph_2MX have been by no means fully investigated.

Bellamy and coworkers measured the infrared spectra of a number of compounds containing the Ph_2B group and assigned the intense absorption in the range 1250–1280 cm^{-1} to νPh–B.[46,47] However, fairly complete spectra and their interpretation have been published very recently. Nahm et al.[48] measured the infrared spectra of a series of compounds Ph_2BX, where X = F, Cl, Br, or I, and assigned the principal bands by comparing these spectra with one another and with the literature data[49]. Measurements have been made[12] of the infrared spectra of a number of compounds Ph_2MX (M = B, Al, or Ga; X = Cl or Br) in the range 200–2000 cm^{-1} and they have been interpreted with the aid of calculations of the frequencies and modes of the in-plane vibrations for a model with C_{2v} symmetry. Analysis of the experimental and calculated data indicates a strong interaction between the vibrations of the Ph–M and M–X groups. There is particularly strong mixing of the r and ν_{B-X} vibrations in the Ph_2BX spectrum, t and ν_{Al-X} in the Ph_2AlX spectrum, and t, u, and ν_{Ga-X} vibrations in the Ph_2GaX spectrum. Additional difficulties arise in the interpretation of the spectra of the gallium and aluminium compounds as a result of their dimerisation[45].

Table 7. Experimental and calculated frequencies (wave-numbers, cm^{-1}) of the M-sensitive vibrations in the spectra of Ph_3M (M = ^{10}B, ^{11}B, Al, Ga, or In).[12,44]

Designation of vibration according to Whiffen (Ref.5)	Vibration symmetry (D_{3h})	Ph_3B i.r. spectra	Ph_3B Raman spectra	Ph_3B calc. (D_{3h})	Ph_3Al i.r. spectra	Ph_3Al calc. (D_{3h})	Ph_3Ga i.r. spectra	Ph_3Ga calc. (D_{3h})	Ph_3In i.r. spectra	Ph_3In calc. (D_{3h})
q	E′	^{10}B 1248 ^{11}B 1235	1240 m(d)	1269 1250	1085 —	1075 —	1080	1069	1070	1065
	A_1'		1145 (s(p)	1160	—	1105	—	1072	—	1070
r	E′	^{10}B 895 ^{11}B 880	— —	910 895	— 670	— 710	— 665	690	673	685
	A_1'		690 s(p)	700	—	703	—	700		702
t	E′	^{10}B 650 ^{11}B 635	— —	630 625	— 425	— 452	— 315	335	270	260
	A_1'	—	255 m(p)	250	—	230	215	215	—	210
u	E′	^{10}B 408 ^{11}B 400	— —	425	332	310	—	250	248	240
	A_2'	—	—	300	—	220	225	207	195	185
y	E″,A_2''	—	—	—	460	—	440 445 453		446	—

Deacon and Green[50] investigated the infrared spectra of Ph_2TlBr in the range 200–3650 cm^{-1} and Srivastava et al.[51] extended this study to a series of compounds Ph_2TlX (X = Cl, CN, CNO, NCS, N_3, NO_2, etc.). The differences in the assignments by these two groups of investigators concern mainly two infrared bands. Deacon and Green[50] assigned a weak band near 1063 cm^{-1} to the q-vibration and a band near 230 cm^{-1} to the u-vibrations, while Srivastava assigned an intense band at 1020 cm^{-1} to the q-vibration and interpreted the 230 cm^{-1} band as a second component of the u-vibration.

The experimental and calculated wave-numbers of the M-sensitive vibrations of compounds with the general formula Ph_2MX are compiled in Table 8.

3. Compounds of the Type $PhMX_2$

The planar structure of the $PhBCl_2$ molecule was demonstrated by electron diffraction[52] and this is probably also true of the Br and I derivatives. If this is so, they have the C_{2v} symmetry and their infrared spectra should show all the vibrations except A_2.

The compounds $PhAlX_2$ and $PhGaX_2$ are associated into cyclic dimers with bridging M–X–M bonds, which should lead to a distortion of the geometry of an individual molecule and to changes in the vibration spectra[45].

The vibration spectra of boron derivatives have been investigated in greatest detail. Thus Butcher and Gerrard[53] measured the infrared spectra of $PhBCl_2$ and $PhBBr_2$ in the range 400–4000 cm^{-1} and assigned the principal bands. An intense 1215–1236 cm^{-1} band was assigned to Ph–B stretching vibrations and bands in the range 850–960 cm^{-1} were assigned to the symmetric and antisymmetric vibrations of the group BX_2.

Greenwood and Wright[54] supplemented these investigations by a study of the infrared spectra of $PhBF_2$. They noted an appreciable increase of the wave-number of the Ph–B stretching vibrations (1292, 1300 cm^{-1}) and detected the vibrations of the BF_2 group in the range 1340–1380 cm^{-1}. The increase of νPh–B was explained by the partial double bond character of Ph–B owing to the delocalisation of the ring π electrons and the P_π non-bonding electron of fluorine via the vacant p orbital of the boron atom. Lockhart[55,56] measured the infrared and Raman spectra of the $PhB^{35}Cl_2$, $PhB^{35}Cl^{37}Cl$, $PhBBr_2$, and PhBBrCl over a wide range (20–1650 cm^{-1}) and carried

Table 8. Experimental (infrared) and calculated frequencies (wave-numbers, cm^{-1}) of the M-sensitive vibrations of compounds of the type Ph_2MX (M = B, Al, or Ga; X = F, Cl, Br, or I).

Designation of vibration according to Whiffen (Ref.5)	Vibration symmetry (C_{2v})	Ph_2BF i.r. spectra (Ref.48)	Ph_2BCl (Ref.12) i.r. spectra	Ph_2BCl (Ref.12) calc.	Ph_2BBr (Ref.12) i.r. spectra	Ph_2BBr (Ref.12) calc.	Ph_2BI i.r. spectra (Ref.48)	Ph_2AlCl (Ref.12) i.r. spectra	Ph_2AlCl (Ref.12) calc.	Ph_2AlBr (Ref.12) i.r. spectra	Ph_2AlBr (Ref.12) calc.	Ph_2GaCl (Ref.12) i.r. spectra	Ph_2GaCl (Ref.12) calc.	Ph_2GaBr (Ref.12) i.r. spectra	Ph_2GaBr (Ref.12) calc.	Ph_2TlCl i.r. spectra (Ref.52)	Ph_2TlBr i.r. spectra (Ref.55)
q	B_1	1375 m.	1250 s.	1285	1260 s.	1280	1260 s.	1095 s.	1090	1095 s.	1085	1090 s.	1072	1090 s.	1072	1015	1063
	A_1	1338 m.	1185 s.	1168	1167 s.	1165	1166 s.	1085 s.	1080	1085 s.	1075	1070 s.	1069	1070 s.	1069		
r	B_1		896 m.	915	892 m.	910	887 m.	675 s.	715	675 s.	715	675 s.	700	670 s.	700		668
	A_1		663 m.	685		675			700		700		690		690		
t	B_1	671 w.	630 m.	635	647 s.	630	633 m.	490 s.	505	450 s	500	335 m.	360	320 m.	355	255	253
	A_1	582 w.	580 m.		580 s.		571 m.		260		230	255 w.	250	245 w.	220	240	
u	B_1		308 w.	308		300			250		245	230 w.	220	210 w.	220		231
				300					230		210		205		195		
y	B_2		600					450 s.		455 s.		453 s.		445 s.		452	450
			545							445 s.		448 s.				438	
ν_{MX}	A_1	1348	910 s.	905	837 s.		811 s.	490 s.	480	450 s.	460	335 m.	340	295 m.	310		

Table 9. Experimental and calculated frequencies (wave-numbers, cm^{-1}) of the M-sensitive vibrations of molecules of the type $PhMX_2$ (M = B, Al, or Ga; X = F, Cl, Br, or I).

Designation of vibration according to Whiffen (Ref.5)	Vibration symmetry (C_{2v})	$PhBF_2$	$PhBCl_2$ (Ref.58)		$PhBBr_2$ (Ref.58)		$PhBI_2$	$PhAlCl_2$ (Ref.58)		$PhAlBr_2$ (Ref.58)		$PhGaCl_2$ (Ref.58)		$PhGaBr_2$ (Ref.58)	
		i.r. spectra (Ref.54)	i.r. spectra	calc.	i.r. spectra	calc.	i.r. spectra (Ref. 48)	i.r. spectra	calc.	i.r. spectra	calc.	i.r. spectra	calc.	i.r. spectra	calc.
q	A_1	1292	1225	1210	1220	1205	1208	1095	1080	1090	1080	1090	1073	1085	1073
r	A_1	—	895	880	880	865	—	675	700	670	700	674	690	670	690
t	A_1	559	632 380	650 ** 355	622	635	585	475 350	482 (460)* 295 (360)	405	432 (405) 220	390	397 (392)	315 300	320(312)
u	B_1	—	330	320	255	270	—	255	260	210	185	228	270	240	210
y	B_2	643	550 475	542 490	525 450	525 472	—	—	—	—	—	—	—	—	—
ν_{M-X}	B_1	1382	915	905	850	827	717	475	495 (465)	405	422 (395)	390	400 (380)	315 300	335 (315)
	A_1	1344	632 380	650 ** 355	622 270	635 240	691	475 350	482 (460) 295 (360)	405	432 (405) 220	390 315	397 (392) 290 (300)	315 300 250	320 218(237)

*The wave-numbers calculated for the model with tetrahedral CMX angles are given in brackets.

**According to the calculation two moles contribute, making the vibrations $t_{A_1} + \nu^{A_1}_{M-X}$.

out a complete assignment of the observed bands. The differences between the band assignments in the $PhBCl_2$ and $PhBr_2$ spectra by the two groups of investigators[53,55] concern mainly the position of the νS band of BX_2.

Nahm et al.[48] studied the infrared spectra (250–4000 cm^{-1}) of a series of compounds $PhBX_2$, where X = F, Cl, Br, or I, and Lee[57] described the infrared spectrum of $PhTlX_2$.

The present author and his coworkers[58] investigated experimentally (infrared spectra) and theoretically (calculation of the frequencies and modes of the normal vibrations) a series of compounds of the type $PhMX_2$ (where M = B, Al, or Ga; X = Cl or Br). Analysis of the results enabled the authors to refine the band assignments in the spectra of boron derivatives and to follow the variation of the frequencies and modes of the M-sensitive vibrations on replacement of M and X.

Stephenson and Coburu[98] discussed certain questions of the structure of the compounds and their dimers on the basis of calculations for planar and tetrahedral conformations of the gallium and aluminium derivatives and a comparison of the infrared spectra with the available[59–64] infrared and Raman spectra of the dimers $(AlX_3)_2$ and $(GaX_3)_2$.[59–64] Table 9 lists the experimental and calculated wave-numbers of the M-sensitive vibrations of a series of compounds of the type $PhMX_2$.

VI. VIBRATION SPECTRA AND STRUCTURES OF PHENYL DERIVATIVES OF GROUP IVB ELEMENTS

Numerous studies have been made on the vibration spectra of compounds of the type $PH_4 - nMX_n$ (where M = C, Si, Ge, Sn, or Pb; X = Cl, Br, or I; n = 0, 1, 2, 3, or 4), but here too there are contradictions in the interpretation and many of the investigations do not include the long-wavelength part of the spectrum, which is particularly important for heavy elements.

1. Compounds of the type Ph_4M

X-Ray diffraction studies showed that crystalline Ph_4C,[65] Ph_4Si,[66] Ph_4Ge,[67] and Ph_4Sn[68] have a central C_4M unit with a tetrahedral structure (T_d symmetry) with the overall molecular symmetry reduced to S_4 when the disposition of the phenyl groups is taken into account. Such decrease of symmetry from T_d to S_4 should be reflected in the infrared spectra primarily by a lifting of the prohibition of symmetrical class A_1 vibrations in the infrared. However, the majority of studies on the vibration spectra of the compounds Ph_4M dealt with individual parts of the spectrum[69–74] and the bands observed in the infrared and Raman spectra were interpreted by comparison with the spectra of aliphatic compounds of the same elements[75] or of halogenobenzenes, i.e. in terms of the monosubstituted benzene approximation with C_{2v} symmetry without taking into account the vibrations of the central unit of the molecule and the interaction of different phenyl groups[76].

In later studies by Smith[77,78], Poller and coworkers[79,80], and other investigators[81–83] the vibration spectra of Ph_4M were considered from the standpoint of the overall molecular symmetry and the possible splitting of the M-sensitive vibrations. The present author and his coworkers[84] calculated the wave-numbers and modes of the in-plane vibrations of the Ph_2M fragment with a CMC angle of 109° and M = C, Si, Ge, Sn, or Pb, which largely confirmed the assignments of the M-sensitive vibrations in the above investigations[78–83] and showed the necessity to take into account the overall molecular symmetry.

Table 10 presents the experimental wave-numbers of the M-sensitive vibrations for Ph_4M molecules and the values calculated for the Ph_2M fragment.

2. Compounds of the Type Ph_3MX

We were unable to find in the literature any direct data concerning the compounds of the type Ph_3MX. The central unit most probably has a tetrahedral structure with C_{3v} or C_3 molecular symmetry. In this case both components of the M-sensitive vibrations (A and E) should be active in the infrared and Raman spectra. The differences in the spectra on passing from C_{3v} to C_3 symmetry are probably small.

A number of workers investigated the vibration spectra of Ph_3MX, where M = C, Si, Ge, Sn, or Pb; X = H, D, Cl, Br, etc., but, as for Ph_4M molecules, most of the investigations dealt only with individual sections of the spectrum and the assignments were made by analogy with monosubstituted benzenes (C_{2v} symmetry).

The infrared spectra of a number of compounds containing the Ph_3C group have been measured[69,85-87] and two bands, at 1185 and 1280 cm^{-1}, have been assigned to the C_6H_5-C stretching vibrations; these vibrations were found to depend little on the substituent X. On the basis of the $^{12}C \rightarrow {}^{13}C$ isotopic shift, Weston et al.[88] assigned only one infrared band to the stretching vibration, this is near 1192, 1202, and 1211 cm^{-1} for Ph_3CH, Ph_3COH, and Ph_3CCl respectively.

Table 10. Experimental and calculated frequencies (wave-numbers, cm^{-1}) of the M-sensitive vibrations in the spectra of Ph_4M (M = C, Si, Ge, Sn, or Pb).

Designation of vibration	Vibration symmetry (S_4)	Ph_4C		Ph_4Si		Ph_4Ge		Ph_4Sn		Ph_4Pb	
		expt. (Ref. 87)	calc.* (Ref. 81)	expt. (Ref. 78)	calc.* (Ref. 84)	expt. (Ref. 81)	calc.* (Ref. 84)	expt. (Refs. 78,82)	calc.* (Ref. 84)	expt. (Refs. 82,83)	calc.* (Ref. 84)
q	E	1260	1220	1108	1105	1033	1086	1075	1085	1060	1080
	A	1190	1205	1100	1085	1030	1070	1062	1069	1063	1065
r	E	—	860	710	716	675	690	682	688	668	683
	A	—	820	700	700	655	673	—	671	645	665
t	E	635	590	435	425	332	305	268	260	225	226
	A	240	253	235	228	222	217	214	210	200	193
u	E	332	350	261	228	232	319	225	275	181	240
	B	292	180	223	215	214	204		195		187
y	E	527	—	520	—	480	—	460	—	450	—
	B	492		510		465		448		440	
x	E	200	—	185	—	187	—	193	—	147	—
	B			170		168		152			

*The calculation was performed for the Ph_2M model with the angle $\alpha = 109°$.

Kriegsmann and Schowtka[71] assigned the 490–515 cm^{-1} bands in the spectra of Ph_3SiX (where X = H, F, Cl, or OH) to $\nu Ph-Si$ (ν_{as}) and Smith assigned the 420–445 cm^{-1} and 330 cm^{-1} bands to t_E- and t_A-vibrations respectively[72].

Later Smith[77] made a detailed study of the infrared and Raman spectra of Ph_3SiX and the Si-sensitive vibrations listed in Table 11 were taken from his communication. The infrared spectra of compounds of the type PhGeX in the range 200–2500 cm^{-1} were reported by Cross and Glockling[89] and by Mackay et al.[90], while Durig et al.[91] extended the infrared range to 33 cm^{-1} and investigated the Raman spectrum; on this basis, they assigned the Ge-sensitive bands (the A and E components).

The vibration spectra of Ph_3SnX were studied by a number of workers[70,73-75,79-83,85-92]. Kriegsmann measured the infrared and Raman spectra of Ph_3SnX (where X = OH, Cl, Br, or I).[75,93,94]. Harrah and Ryan[95] interpreted the spectra of a number of aromatic organotin compounds and extended the measurements to 200 cm^{-1}.

Poller made a detailed study of the $Ph_{4-n}SnX_n$ (where X = Cl or Br; n = 1, 2, 3, or 4) spectra[79] and his assignments have been confirmed by other workers[80,92,96].

Clark et al.[83] investigated the infrared and Raman spectra of Ph_3PbX (where X = F, Cl, Br, or I) and assigned the observed bands. From the shift of certain Pb-sensitive bands in different states of aggregation, the authors deduced that the compounds are monomeric in benzene solutions and associated in crystals.

3. Compounds of the Type Ph_2MX_2

There are almost no experimental data concerning the structure of compounds of this type. Keidel and Bauer[85] suggest that Ph_2SiCl_2 has C_2 symmetry. The M-sensitive vibrations should then be split into A and B components active in the infrared and Raman spectra. A more complex crystalline structure, consisting of planar Cl_2PbCl_2 cells containing equivalent Pb–Cl bonds with the phenyl groups at right angles to the axis of the ring and bonds approximately perpendicular to the plane of the ring, has been described for Ph_2PbCl_2.[87]

Table 11. Experimental frequencies (wave-numbers, cm^{-1}) of the M-sensitive vibrations in the spectra of Ph_3MCl and Ph_2MCl_2 (M = C, Si, Ge, Sn, or Pb).

Designation of vibration according to Whiffen (Ref.5)	Vibration symmetry (C_{3v})	Ph_3MCl					Vibration symmetry (C_{2v})	Ph_2MCl_2			
		C (Ref. 88)	Si (Ref. 77)	Ge (Ref. 91)	Sn (Ref. 79)	Pb (Ref. 83)		Si (Ref. 77)	Ge (Ref. 90)	Sn (Ref. 80)	Pb (Ref. 83)
q	E	1210	1117	1094	—	1058	B_1	1120	1095	—	1052
	A_1		1102				A_1	1102	1088	—	
r	E	845	716	678	—	687	B_1	717	680	—	652
	A_1	818	700	665	—	—	A_1	697	671	—	
t	E	635	434	329	270	235,225	B_1	444	332	275	236
	A_1	(263)	306	273	240	200	A_1	318	270	230	195
u	E	311	250	250	217	175	B_1	283	—	—	167
	A_1		240	232	210		A_1	245	270	—	—
y	E	503	504	469	450	448	B_2	480	453	—	—
	A_1			460	442	441			420	444	445
						438					
ν_{M-X}	A_1	746	552	375	335	290	B_1	576	398	365	—
		735					A_1	548		356	

The vibration spectra of Ph_2CH_2, Ph_2SiX_2 (X = H, CH_3, F, Cl, or OH,[71,72,77,78,90] Ph_2GeX_2 (X = Cl or Br),[90] Ph_2SnX_2 (X = Cl, Br, or I),[73,80,90] and Ph_2PbX_2 (X = Cl, Br, or I)[84] have been investigated experimentally[78,97]. The M-sensitive vibrations of these compounds are listed in Table 11.

4. Compounds of the Type $PhMX_3$

It has been shown by electron diffraction that $PhMX_3$ molecules have a CMX_3 tetrahedral framework and the C_{3v} symmetry has been assigned to them[23]. Calculation of the normal vibration modes for molecules of the type $PhMX_2$, where M is a Group IIIB element, showed that the M-sensitive vibrations do not have the character of individual group vibration and include to a greater or lesser extent the vibrations of all the atoms of the central unit[58]. However, in analysing the vibration spectra of $PhMX_3$, most workers consider separately the vibrations of the Ph–M (C_{2v} symmetry) and MX_3 (C_{3v} symmetry) groups and observe the non-split q-, r-, t-, u- and x-vibrations of monosubstituted benzene and the symmetrical and degenerate vibrations of the MX_3 groups.

The vibration spectra of $PhCH_3$, its deuteriated analogues, and $PhCCl_3$ have been investigated in detail by a number of workers[98-100] and have been fully interpreted from an analysis using experimental infrared, Raman spectroscopic, and calculated data.

The infrared and Raman spectra of $PhSiX_3$, where X = F, Cl, or H, have been studied[71]. Smith extended the investigation of the infrared spectra of these compounds initially to 250 cm^{-1} [72,77] and later to 50 cm^{-1}.[73]

Durig et al.[101] supplemented these studies by investigating the Raman spectra of $PhSiCl_3$. The same

workers[78,101] and also Jakoubkova and Hetflejs[102] made a detailed study of the vibration spectra of $PhGeCl_3$; Durig and Sink[103] obtained and analysed in detail the infrared and Raman spectra of $PhGeCl_3$. The infrared spectra of $PhSnCl_3$ have been investigated up to 400 cm^{-1} [70,73] and subsequently the range was extended to 50 cm^{-1} (Smith[78]) and the Raman spectra were also studied[101].

Table 12. Experimental frequencies (wave-numbers, cm^{-1}) of the M-sensitive vibrations in the spectra of $PhMCl_3$ (M = C, Si, Ge, Sn, or Pb).

Designation of vibration according to Whiffen (Ref.5)	$PhCCl_3$ (Ref.98)		$PhSiCl_3$		$PhGeCl_3$		$PhSnCl_3$		$PhPbCl_3$
	i.r. spectra	Raman spectra	i.r. spectra (Ref.78)	Raman spectra (Ref.101)	i.r. spectra (Ref. 78)	Raman spectra (Ref. 101)	i.r. spectra (Ref. 78)	Raman spectra (Ref.101)	i.r. spectra (Ref. 83)
q	1188	1184	1118	1122	1088	1085	1067	1067	1052
r	627	630	714	719	674	677	662	660	652
t	308	307	346		290		250		240
u		246	284	248	255	214	218	184	170
y	507	506	460		454		439		445
ν_{M-xE}	790	788	584		429		377		—
ν_{M-xA}				518		407		363	—

Table 12 lists the wave-numbers assigned to the M-sensitive vibrations.

VII. VIBRATION SPECTRA AND STRUCTURES OF PHENYL DERIVATIVES OF GROUP VB ELEMENTS

A pyramidal structure is characteristic of Group VB elements in the tervalent state. The angle between the bonds at the vertices of the pyramid depends on the nature of the group joined to the element. In aromatic derivatives the CMC angle is reduced from 116° ± 2° in Ph_3N (Sasaki et al.[104]) to 103° in Ph_3P (Daly[105]) and 96° in Ph_3As (Gullen and Hochstrasser[106]), which has been attributed to different degrees of conjugation. The overall symmetry of molecules of this type depends on the structure of the groups combined with the elements.

1. Compounds of the Type Ph_3M

As stated above molecules of this type are pyramidal and, for the same phenyl substituents, the central MC_3 unit should have C_{3v} symmetry. However, it has been shown[104,105] that the overall symmetry of such molecules is reduced to C_3 owing to the rotation of the planes of the rings. Such molecular symmetry should lead to the activity of the class A and E vibrations to which all M-sensitive vibrations belong, both in the infrared and Raman spectrum, and in the latter the class A vibrations should be polarised.

Despite the large-scale employment of aromatic nitrogen derivatives in the chemistry of dyes and in photochemical research, the vibration spectra or even the simplest derivative Ph_3N have been studied very incompletely. As a rule, only the positions of individual bands have been determined in the spectra of tertiary aromatic amines.

Thus, having analysed the infrared spectra of a large number of tertiary aromatic amines, Bellamy[107], Ritschl[108], and Katritzky and Jones[109] assigned the intense bands in the range 1210–1340 cm^{-1} to νPh–N stretching vibrations and noted that the positions of the bands depend on the electron-accepting properties of the ring substituents.

Colthup[110] assigned the medium-intensity band near 1275 cm^{-1} in the infrared spectrum of Ph_3N to νPh–N. Since account must be taken of the possibility of the splitting of the M-sensitive vibrations of the Ph_3N molecule, the infrared band discovered by Colthup should probably be assigned to the E component of the q-vibration. However, the q_A-component has never been observed, although it should be active in the infrared for C_{3v} or C_3 symmetry. Colthup's studies on the infrared and Raman spectra with polarisation and also calculations on the A and E class vibrations of Ph_3N made it possible to assign to the q_E- and q_A-vibrations an intense infrared and depolarised Raman band near 1280 cm^{-1} and a weak infrared band and intense and highly polarised Raman line near 1175 cm^{-1}.[44] These data indicate a small deviation of the central Ph–N bonds from the plane and suggest the possibility of D_3 symmetry for the Ph_3N molecule.

Table 13. Experimental and calculated frequencies (wave-numbers, cm^{-1}) of the M-sensitive vibrations in the spectra of Ph_3M (M = N, P, As, Sb, or Bi).

Designation of vibration according to Whiffen (Ref.5)	Vibration symmetry (C_3)	Ph_3N (Ref.44)			Ph_3P (Ref.111)		Ph_3As (Ref.111)		Ph_3Sb (Ref.111)		Ph_3Bi (Ref.111)	
		expt.		calc. (D_{3h})	expt.							
		i.r. spectra	Raman spectra		i.r spectra	Raman spectra	i.r spectra	Raman spectra	i.r. spectra	Raman spectra	i.r. spectra	Raman spectra
q	E	1280	1280 m(d)	1265	1090 m		1075 m.		1065 m.		1061 m.	
	A		1175 s(p)	1175	1104 w.	1098 s(p)	1082 w.	1086 m(p)		1068 n(p)	1055 m.	1060 w.
r	E	890		890	690 s.	703 m.	668 m.		655 w.		645 w.	650 s.
	A		717 s(p)	720		684 m.		670 s(p)		657 (n)		
t	E	620		630	420 m.	412 m.	310 m.	317 m.	276 m.	276 w.	225 s.	223 m.
	A		290 m(p)	253	255 m.	253 s(p)	242 w.	241 s(p)		224 m(p)	216 m.	210 s.
u	E	435 w.	417 m(d)	465	270 w.	274 w.	233 w.					
	A	325 w.	335 m(d)	365	214 w.	215 w.	192 m.	197 s.	255 s.	259 w.	235 m. 199	236 200
y	E, A	515 503			513 s. 500 s. 490 s.	502 m.	473 m. 468 s.		462 m. 450 s. 446 m.	460 w.	450 s. 435 m.	
x	E, A	242	250		196 186	202 191	192 m. 184 w.	197 s.	179 160	178 168	166 146	166

In recent years a number of studies have been made on the vibration spectra of triphenyl compounds of phosphorus[76,95,105,111–123], arsenic[76,95,111,117,119,123–127], antimony[76,95,111,123,128], and bismuth[76,95,111]. However, despite a fairly large number of investigations and the availability of data not only for infrared but also for Raman spectra with polarisation, the observed bands were as a rule assigned to specific vibrations in terms of the monosubstituted benzene approximation. The possible splittings of the M-sensitive vibrations were discussed only in later studies by Green and coworkers[118,125,126]. Table 13 lists the M-sensitive bands.

It is noteworthy that, in contrast to Ph_3N, in the infrared spectrum of which the A components of the M-sensitive vibrations are inactive (approximate D_3 symmetry), both components are as a rule observed in the infrared spectra

of the compounds Ph_3M, where M = P, As, or Sb. This can be traced particularly clearly for the components of the *t*-vibrations.

2. Compounds of the Type Ph_2MX

It has been shown by electron diffraction that aliphatic derivatives of Group VB elements of the type $(CH_3)_2MX$ have C_S symmetry [23]. Similar conclusions have been reached concerning the structure of aromatic derivatives on the basis of polarisation data for Raman spectra. In the case of C_s symmetry all the vibrations should be observed in the infrared and Raman spectra and therefore the infrared spectra should show both components of the M-sensitive vibrations.

Bellamy [107] and Katritzky and Jones [109] assigned to the Ph–N vibrations the intense infrared bands of Ph_2NH and Ph_2NCH_3 in the range 1280–1350 cm^{-1}, increasing to 1370 cm^{-1} in Ph_2ND as a result of interaction with N–D deformation vibrations [129].

Bearing in mind the smallness of the deviation from planarity of the C_3N central unit in Ph_3N, we calculated the wave-numbers and modes of the vibrations of the planar Ph_2NCH_3 model (C_{2v} symmetry). [130] The principal bands were assigned by comparison of the infrared spectra of Ph_3N and Ph_2NCH_3 and calculations on the vibrations of these molecules.

The vibration spectra of Ph_2PH, [115,131] Ph_2AsH, [131] Ph_2PCl, [122,132] Ph_2AsCl, Ph_2AsBr, [127] and Ph_2AsCH_3 [125,126] were investigated in a number of studies. Analysis of the infrared and Raman spectra of most of these compounds made it possible to separate the M-sensitive vibrations, which are listed in Table 14.

Table 14. Experimental frequencies (wave-numbers, cm^{-1}) of the M-sensitive vibrations in the spectra of Ph_2MX and $PhMX_2$.

Designation of vibration according to Whiffen (Ref.5)	Vibration symmetry (C_s)	Ph_2NCH_3	Ph_2PCl		Ph_2AsCl		PhN $(CH_3)_2$	$PhPCl_2$		$PhAsCl_2$	
		i.r. spectra (Ref. 130)	i.r. spectra (Ref. 132)	Raman spectra (Ref.132)	i.r. spectra (Ref. 127)	Raman spectra (Ref.127)	i.r. spectra (Ref. 130)	i.r. spectra (Ref. 132)	Raman spectra (Ref.132)	i.r. spectra (Ref. 132)	Raman spectra (Ref.132)
q	A″	1282 s.	1096 s.		1075						
	A′	1250 s.		1099 w(p)		1082	1230 s.	1085 s.	1087 w(p)	1076	1077
r	A″	865 s.	700 s.		668						
	A′	785 m.		693 w(p)		672	810 w.	699 s.	698 w(p)	672	677
t	A″	593 m.	404 s.		312	320	525 w.				
	A′	567 s.		285 w(p)	301	302			290 m(p)	307	312
u	A″					248	465 w.				254
	A′					218					227
y	A″	510 m.	462 m.		473 460	479 465	515 m.	460 s	460 m(d)	460	465
νM–X	A′ (A′, A″)	953 m.	593 s. 462 m.		372	372	1060 m. 945 m.	500 s. 460 s.	500 m(p) 460 m(d)	368 390	369 393

3. Compounds of the Type $PhMX_2$

It has been shown by electron diffraction that in the vapour phase $PhNH_2$ has the C_S symmetry and therefore the N-sensitive vibrations are active in both infrared and Raman spectra. Bellamy [107] and Katritzky and Jones [109] assigned to νPh–N a band in the range 1250–1340 cm^{-1} in the infrared spectra of a large series of primary aromatic amines. Ritschl and Kunkel [133] studied the infrared spectra of 18 *para*- and *meta*-substituted dimethylanilines and assigned the 1340 cm^{-1} band to the Ph–N vibrations and the 1057 and 943 cm^{-1} bands to the ν_{as} and ν_s vibrations of the CH_3–N group. On the basis of the $^{14}N \rightarrow {}^{15}N$ isotopic shift, Tsuboi assigned the 1276 cm^{-1} infrared band of $Ph^{15}NH_2$ to the stretching vibration of the Ph–N group. [134]

According to Evans's data [135], this band should be regarded as due to the *q*-vibration. The remaining N-sensitive vibrations have been much less studied. The infrared and Raman spectra of $PhPH_2$, [121,131] $PhAsH_2$, [131] $PhPCl_2$, [122,132] $PhAsCl_2$, [127,132] $PhAsBr_2$, [127] and $PhAs(CH_3)_2$, [125,126] have been studied in a number of investigations. Table 14 lists the vibrations assigned to the PhM and MX_2 groups.

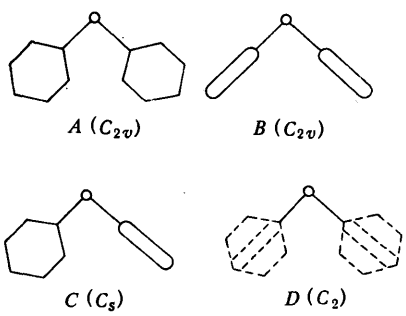
Analysis of the vibration spectra has confirmed the C_S symmetry of the molecules investigated [121,131,132,135]. The barrier to rotation of the C–N bond in the $PhNH_2$ molecule (3.54 kcal $mole^{-1}$) and the barrier to inversion at the nitrogen atom (4.5 kcal $mole^{-1}$) have been estimated [135].

VIII. VIBRATION SPECTRA AND STRUCTURES OF PHENYL DERIVATIVES OF GROUP VIB ELEMENTS

Aromatic derivatives of Group VIB elements in the crystalline state have an R–M–R central unit with a bent structure ($\alpha < 180°$) and the planes of the benzene rings are rotated relative to one another by an angle φ. The angles depend on the central atom M and are $\alpha = 123° \pm 2°$ for $(p\text{-Br–}C_6H_4)_2O$, [23] $\alpha = 109°$ and $\varphi = 56°$ for $(p\text{-}CH_3C_6H_4)_2S$, [138] $\alpha = 106°$ and $\varphi = 55°$ for $(p\text{-}CH_3C_6H_4)_2Se$, [139] and $\alpha = 101°$ and $\varphi = 62°$ for $(p\text{-}CH_3C_6H_4)_2Te$. [140]

Compounds of the Type Ph_2M

When discussing the vibration spectra of molecules of this type, one considers several configurations differing in the disposition of the benzene rings relative to one another and referring to different symmetry species:



As for the phenyl derivatives of the elements of other Groups, some investigators interpret the vibration spectra of the compounds examined in this section in terms of the monosubstituted benzene approximation without taking into account the interactions of two phenyl groups via the M atom [137]. Katon and Feairheller [141] and Green [142] believe that the asymmetric configuration C (C_S symmetry) is the most probable and interpret the vibration

spectra of Ph_2O and Ph_2S from the standpoint of the presence of two non-equivalent weakly interacting rings: the π orbitals of one ring overlap with those of the O or S atoms, while the second ring is not involved in such overlapping. On this basis, different M-sensitive vibrations are assigned to each benzene ring. However, other investigators concluded from a comparison of the polarisabilities and dipole moments [143] and also an analysis of the infrared, Raman, and NMR spectra [147] that the rings in these molecules are fairly mobile and therefore the B and D configurations with equivalent rings are probable for Ph_2M. The present author's calculation on class A_1 and B_1 vibrations of the A and B models of the Ph_2O and Ph_2S molecules [136] permits an interpretation of the bands which have been assigned [142,143] to the M-sensitive vibrations of two non-equivalent rings, being the symmetric and antisymmetric components of these vibrations. However, it has been shown that the contributions of the first and second rings of model C to the M-sensitive vibrations are in fact non-equivalent.

The vibration spectra of the phenyl derivatives of selenium and tellurium have been hardly investigated. Fritz and Keller [137] measured the infrared spectra of a number of O, S, Se, and Te derivatives in the range 250 to 3500 cm^{-1}, but the spectra are quoted almost without interpretation. The authors assigned bands near 455 to 487 cm^{-1} to Ph–Te vibrations.

Table 15. Experimental and calculated frequencies (wave-numbers, cm^{-1}) of the M-sensitive vibrations in the spectra of Ph_2M (M = O, S, Se, or Te).

Designation of vibration according to Whiffen (Ref.5)	Vibration symmetry (C_2)	Ph_2O			Ph_2S			Ph_2Se		Ph_2Te	
		i.r. spectra (Ref.6)	Raman spectra (Ref.6)	calc. for 120° (Ref.136)	i.r. spectra (Ref.7)	Raman spectra (Ref.7)	calc. for 110° (Ref.136)	i.r. spectra (Ref.137)	calc. for 105° (Ref.107)	i.r. spectra (Ref.137)	calc. for 100° (Ref.136)
q	B	1236 s.	1240 w.	1238	1083 s.	1093 s.	1075	1064 m.	1070	1063 w.	1069
	A	1198 m.	1200 m(p)	1205	1085 s.	1095 s(p)	1097	1085 m.	1085		1082
r	B	866 s.	868 w.	850	688 s.	696 s.	690	665 s.	672	662 s.	670
	A	798 s.	800 m(p)	785	700 w.	696 s(p)	700	687 s.	685		685
t	B	563 w.	568 m.	550	412 w.	412 w.	402	318 m.	305	255 s.	255
	A	314 w.	315 m(p)	290	270 w.	270 m(p)	280		266	202 w.	208
u	B	498 s.	508 w.	535	412 w.	412 w(d)	403		230	274 w.	266
	A	412 w.	418 w(p)	422 290	214	213 m(d)	220		220	188 s. 146 w.	218
x	B										
y	B	498 s. 480 s. 478 s	485 w.		519 s. 466 s.			479 s. 456 s.		460 s. 445 s.	

McWhinnie and coworkers [145] assigned the 255 and 202 cm^{-1} bands in the infrared and Raman spectra of Ph_2Te_2 to the asymmetric and symmetrical Ph–Te vibrations respectively. The present authors' calculations of the wave-numbers and modes of the in-plane normal vibrations of the Ph_2Se and Ph_2Te molecules [18], using experimental spectra [137] and structural data [139,140], make it possible to assign the bands in Table 15 to the Se- and Te-sensitive vibrations.

Analysis of the experimental and calculated data for the vibration spectra of aromatic derivatives of the elements permits certain general conclusions.

1. For the vibration spectra to yield sufficiently complete information concerning the structure of aromatic derivatives of the elements, the influence of the nature of the element, and of the degree of complex formation, it is necessary to take into account the overall molecular symmetry and the possible interaction of the substituents via the atom of the element. The monosubstituted benzene approximation employed in the majority of investigations is inadequate for polyvalent elements.

2. Calculations on the vibrations of the phenyl derivatives of Group I–VI elements have established a general relation governing the dependence of the force constants K_{Ph-M} on the position of the element in the Periodic System (Table 16).

Table 16. The force constants K_{Ph-M} for Ph_nM (in units of 10^6 cm^{-1}).

Li 1.2	Be 6.7	B 6.5	C 6.5	N 7.5	O 7.5	F 9.0
	Mg 3.2	Al 3.7	Si 4.3	P 4.12	S 4.1	Cl 5.8
	Zn 3.7	Ga 3.82	Ge 3.8	As	Se 3.7	Br 4.8
	Cd 3.5	In 3.6	Sn 3.65	Sb	Te 3.55	I 3.9
	Hg 3.7	Tl	Pb 3.5	Bi		

Note. The K_{Ph-M} were obtained for derivatives of Group I, III, and V elements [12,44], Group II and VI elements [18], Group IV elements (Ph_2M model with $\angle CMC = 109°$), [84] and Group VII elements [3] using a conversion factor of 1.56.

The principal, most significant change in K_{Ph-M} is its decrease within each Group on passing from elements of the Second Period to those of the Third, Fourth, etc. Periods, K_{Ph-M} decreasing most markedly on passing from elements of the Second Period to those of the Third Period.

Analysis of the published data on the force constants K_{C-M} for methyl derivatives of the same elements reveals a qualitatively similar behaviour [137]. This leads to the conclusion that the main factor influencing the value of K_{C-M} is probably the efficiency of the overlapping of the orbitals forming the C–M σ bond which depends significantly on the relative dimensions (principal quantum number) and geometry (hybridisation) of the orbitals of the valence electrons linking the atoms.

3. The Ph–M stretching vibration of the compounds considered here is not characteristic only of the C–M bond and involves to a greater or lesser extent several complex vibrations of the entire molecule (the q-, r-, and t-vibrations according to Whiffen [5]). When several phenyl groups are attached to a polyvalent atom M, each such vibration is split into components, whose number, activity, and the degree of splitting depend on the nature of the element and molecular structure.

4. Analysis of the calculated modes of the q-, r-, and t-vibrations shows that the contribution of ν_{Ph-M} to each of the three vibrations is non-equivalent and depends

mainly on the force constant K_{Ph-M}. When the C–M bond is very rigid ($K_{Ph-M} > 5 \times 10^6$ cm^{-2}), the q- and r-vibrations are most sensitive to the stretching of this bond and to structural changes in the molecule. Under these conditions, the t-vibration hardly includes ν_{Ph-M} and therefore carries little information about the central framework of the molecule. Table 16 shows that derivatives of elements in the Second Period should be regarded as of the same type and that in this case ν_{Ph-M} contributes most to the q- and r-vibrations.

When $K_{Ph-M} < 5 \times 10^6$ cm^{-2}, which is characteristic of derivatives of elements in the Third, Fourth, Fifth, etc. Periods, the contribution of ν_{Ph-M} to the q- and r-vibrations diminishes significantly and these vibrations, having been displaced towards longer wavelengths to 1050–1070 cm^{-1} and 670–700 cm^{-1} respectively, become relatively insensitive to the nature of the element and the rigidity of the C–M bond. On the other hand, ν_{Ph-M} contributes most to the t-vibration in the spectra of such molecules, and for large masses of M (Hg, Tl, Pb, Te, etc.) and low force constants K_{Ph-M} [around $(3.5-3.6) \times 10^6$ cm^{-2}] the t-vibration becomes a virtually pure ν_{Ph-M} vibration.

5. Within each Group of the Periodic System, the force constant K_{Ph-M} varies in the opposite sense to the mass of the element, i.e. K_{Ph-M} as a rule decreases appreciably with increase of the mass of M. Hence follows the rule, discovered by Whiffen, of the dominant contribution of ν_{Ph-M} to the q-vibration of "light" elements and to the t-vibration of "heavy" elements. However, calculation of the vibration modes shows that, when for any reason K_{Ph-M} decreases appreciably in derivatives of a "light" element or increases in derivatives of a "heavy" element, Whiffen's rule ceases to hold. Thus, for the "lightest" of the elements discussed in this review (lithium), as a result of the sharp decrease of K_{Ph-Li} (1.2×10^6 cm^{-2}) due to the polarisation of the C–Li bond and "electron-deficient" binding the experimental and calculated data fail to show an isotopic shift on replacement of lithium-7 by lithium-6 and there is a decreased contribution of ν_{Ph-Li} to the q- and r-vibrations, an appreciable isotopic shift, and a significant contribution of ν_{Ph-Li} to the t-vibration.

6. It is noteworthy that within each Period K_{Ph-M} varies slightly as a function of the electronic nature of the elements belonging to different Groups of the Periodic System, but these changes are comparatively small (with the exception of lithium in the Second Period) and do not lead to the breakdown of Whiffen's rule. If in addition account is taken of the relatively small change of the mass of the elements within the same Period, the possibility of finding the absorption regions of the q-, r-, and t-vibrations for derivatives of any element from the known spectra of the derivatives of another element in the same Period becomes understandable. However, this interpretation fails to take into account molecular structure and is therefore rough and qualitative.

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Karpov Physicochemical
Institute, Moscow

U. D. C. 547.15

Advances in the Chemistry of Stable Hydrocarbon Radicals

V.D.Sholle and E.G.Rozantsev

The current data on the structure of tervalent carbon radicals are examined and their principal spectroscopic characteristics are presented. The latest studies on the synthesis of stable hydrocarbon radicals, including ultrastable perchlorotriarylmethyl radicals, are considered together with classical investigations. In the discussion of chemical properties, much attention has been devoted to the dimerisation of triarylmethyls, since this problem has altered drastically the traditional concept of tervalent carbon radicals. Modern ideas concerning certain hydrocarbon biradicals are presented. The bibliography includes 150 references.

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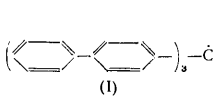
I. INTRODUCTION

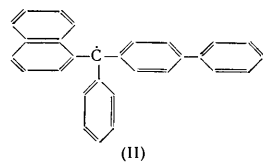
After Gomber's discovery[1] of the triphenylmethyl radical, an enormous number of studies have been published on the chemistry and physics of stable hydrocarbon radicals. Many of them have been analysed in familiar reviews by Soviet and foreign workers[2-4]. However, progress in this field of knowledge has been so great in recent years that many postulates which were believed to be firmly established have become obsolete. Together with classical investigations, the present review deals in detail with the latest studies which have greatly modified the traditional ideas about tervalent carbon radicals.

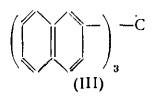
In the literature all stable hydrocarbon radicals are as a rule included under one name — triarylmethyls — which is not altogether correct. It is therefore useful to consider the principal types of stable hydrocarbon radicals before discussing their properties and methods of synthesis.

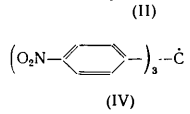
II. PRINCIPAL TYPES OF STABLE HYDROCARBON RADICALS

Gomberg did not synthesise the triphenylmethyl radical but its dimer and it was not until 1909 that Wieland[5] showed that this dimer is in equilibrium with its radical in solution. After establishing the nature of triphenylmethyl, many of its derivatives were synthesised, some of which, namely tri-*p*-biphenylylmethyl (I)[6], *p*-biphenylyl-α-naphthylphenylmethyl (II)[7], tri-β-naphthylmethyl (III)[8], and tri-*p*-nitrophenylmethyl (IV)[9], have been isolated in a crystalline form:

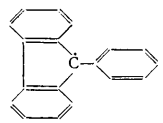

(I)

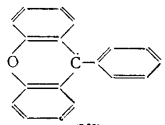

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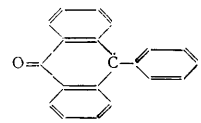

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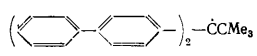

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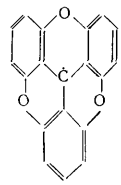
The 9-phenylfluorenyl (V)[6], phenylxanthyl (VI)[10], phenanthronyl (VII)[11], di-*p*-biphenylyl-t-butylmethyl (VIII)[12], and sesquixanthydryl (IX)[13-14] radicals exist in equilibrium with their dimers:


(V)

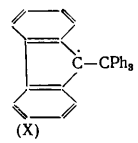

(VI)


(VII)

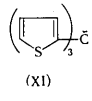

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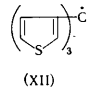

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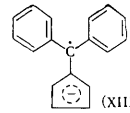
As early as 1922, Schlenk and Mark obtained a higher homologue of triphenylmethyl (pentaphenylmethyl) and its biphenylene analogue (X)[15]:


(X)

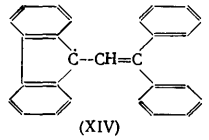
Very stable fluorinated[16-18] and chlorinated[19] derivatives of triphenylmethyl were synthesised recently; analogues of triphenylmethyl radicals were also obtained – trithienylmethyls (XI) and (XII)[20] and the radical-anion of diphenylfulvene (XIII)[21]:

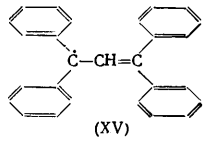

(XI)


(XII)

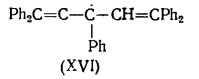

(XIII)

In 1922 Ziegler[22, 23] achieved the synthesis of the allyl radicals (XIV) and (XV), which are examples of a new series of tervalent carbon radicals:


(XIV)

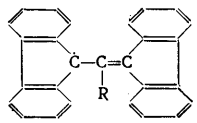

(XV)

Wittig extended this series having synthesised the diallyl and triallyl radicals [(XVI) and (XVII) respectively][24]:

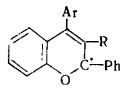

(XVI)

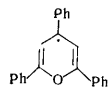

(XVII)

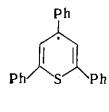
Later Koelsch[25], Solar[26], and Kuhn and coworkers[27, 28] investigated a series of bisbiphenyleneallyl radicals of type (XVIII):

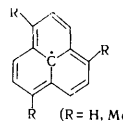

(XVIII) (R=H, Me, Ar)

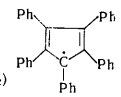
Chromenyl (XIX)[29, 30], pyryl (XX)[31], thiapyryl (XXI)[32], and perinaphthyl (XXII)[33] radicals as well as the highly symmetrical pentaphenylcyclopentadienyl radical (XXIII), which has been isolated in a crystalline form[34], can also be included among radicals of the allyl type:


(XIX) (R = H, Alk, Ar)


(XX)

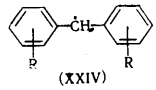

(XXI)


(XXII) (R = H, Me)


(XXIII)

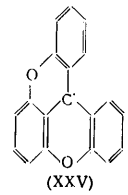
The heterochain radicals $(C_6H_5S)_3C\cdot$ and $CH_3S(C_6H_5S)_2C\cdot$ obtained recently proved to be relatively unstable[35].

Diarylmethyl radicals (XXIV), which have been investigated in detail by Nauta[36, 37] and Theilacker[38], are much less stable than triarylmethyls. Only perchlorodiphenylmethyl has now been isolated in a pure form[39]:


(XXIV)

III. STRUCTURE AND SPECTRA

The electronic spectra of triarylmethyls have two characteristic regions; a region with a very intense absorption at 200 – 400 nm ($\epsilon \simeq 10^4$) and a region of less intense absorption at 500 – 650 nm ($\epsilon \simeq 10^2 - 10^3$)[40]. Triphenylmethyl itself absorbs in the visible region at 484 and 515 nm.[41] Substituents in the *para*-position cause a bathochromic shift of this band, while *ortho*-substituents give rise to a hypsochromic shift owing to the decrease of the coplanarity of the phenyl rings. However, the radical (XXV) absorbs at 490 and 500 nm[42]:


(XXV)

since oxgen bridges prevent the breakdown of coplanarity. The spectrum of 9-phenylfluorenyl (V) is close to that of triphenylmethyl, but the bands are displaced by 800 cm^{-1} towards higher wave-numbers[43]. The electronic spectrum of diphenylmethyl has been interpreted theoretically[44].

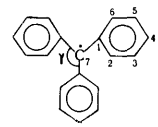
The luminescence spectra of di- and triphenylmethyl radicals were also recorded[45] and showed that diphenylmethyl is more coplanar than triphenylmethyl.

The infrared spectra of tervalent carbon radicals are not characteristic[19, 46].

As expected on symmetry grounds, the dipole moment of triphenylmethyl is close to zero[47].

The earlier quantum-mechanical calculations[48] were based on the hypothesis that the triphenylmethyl molecule is planar. However, it was noted subsequently[49] that account must be taken of the mutual repulsion of the *ortho*-hydrogen atoms. Calculation, taking into account such repulsion, shows that the benzene rings must be rotated relative to the plane of the bonds of the central carbon atom by 30° (the θ angle), i.e. the triphenylmethyl molecule should have the shape of a propeller. In this case the conjugation energy decreases only slightly, while the repulsion energy falls very markedly.

The θ angle in tri-*p*-nitrophenylmethyl, which was determined by X-ray diffraction, proved to be 30°.[50] The value for triphenylmethyl in the gas phase is somethat greater (40 – 45°)[51].



The $C_{(7)} - C_{(1)}$ bond length is 1.48 Å for triphenylmethyl, which is less than in triphenylmethane (1.53 Å). On passing from triphenylmethane to the radical, the angle γ increases from 112° to 118°, which corresponds to a change in the hybridisation of the central atom from sp^3 to sp^2.

The X-ray diffraction patterns of perchlorodiphenylmethyl show that the benzene rings are displaced from the trigonal plane of the central atom[52].

Since di- and triarylmethyls are typical π-electron radicals, their unpaired electron is delocalised over the entire π-bond system, which is clearly reflected in the ESR spectra. The constants for the hyperfine coupling (HFC) with protons, determined from the ESR spectra, are $a_{H(ortho)} = 2.55$ G, $a_{H(meta)} = 1.11$ G, and $a_{H(para)} = 2.78$ G for triphenylmethyl[53]. Similar values were obtained from electron nuclear double resonance (ENOR) spectra[54]. The constant for hyperfine coupling with ^{13}C in the central position is 26 G and the *g*-factor is 2.0026.[55]

More than 50% of the spin density of the unpaired electron is concentrated at the central carbon atom. The spin density is positive in the *ortho*- and *para*-positions of the benzene rings and negative in the *meta*-positions.

para- and *meta*-Substituents have only an insignificant influence on the distribution of spin density, while on introduction of *ortho*-substituents the spin density of the central carbon atom increases and that in the benzene rings decreases[13]. This is due to an increase of the deviation of the benzene rings from coplanarity. An increase of the coplanarity of the rings, as for example in sesquixanthydryl (IX), leads to an increase of $a_{H(para)}$ to 3.17 G.[14]

Table 1. The HFC constants (in gauss) for certain triarylmethyls

Radical	$a_{H(ortho)}$	$a_{H(meta)}$	$a_{H(para)}$	References
$Ph_3\dot{C}$	2.55	1.11	2.78	53
$(p\text{-}FC_6H_4)_3\dot{C}$	2.70	1.13	6.5 (F)	55
$(m\text{-}FC_6H_4)_3\dot{C}$	2.64	1.09 (F)	2.85	55
$(2,6\text{-}F_2C_6H_3)_3\dot{C}$	2.11 (F)	1.06	2.61	57
$(3,5\text{-}F_2C_6H_3)_3\dot{C}$	2.14	1.67 (F)	2.52	57
$(p\text{-}NO_2C_6H_4)_3\dot{C}$	2.50	1.14	0.66 (N)	58
$(p\text{-}MeOC_6H_4)_3\dot{C}$	2.89	1.05	0.34 (Me)	59
$(2,6\text{-}(MeO)_2C_6H_3)_3\dot{C}$	0.14 (Me)	1.06	2.26	13
Sesquixanthydryl(IX)	—	0.39	3.17	14

The unusual ratio $a_{H(ortho)} : a_{H(para)} = 2$ in the 9-phenylthiaxanthyl radical is evidence of the hindered rotation of the phenyl group, the angle of its displacement from the plane of the heterocycle amounting to 72°.[56] Table 1 lists the HFC constants for certain triarylmethyls.

Table 2. The proton HFC constants a_i and spin densities in symmetrical diarylmethyls

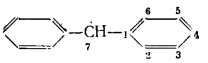
Substituent	a_2	a_3	a_4	a_7	ρ_C^π	References
H	3.05	1.22	3.05	8.36		62
2,6-Me_2	2.15	1.43	3.25	16.27	0.71	63
2,6-Et_2	1.47	1.7	3.17	16.22	0.70	63
2,6-(i-Pr)$_2$	2.22	0.74	2.22	16.69	0.73	63
2-(t-Bu)	3.42	1.37	3.42	15.92	0.69	63
2,5-(t-Bu)$_2$	3.15	1.20	3.50	15.15	0.66	64

The ESR spectrum of perchlorotriphenylmethyl radicals consists of a singlet with satellites due to the ^{13}C nuclei, the *g*-factor amounting to 2.0025. In these radicals, 70% of the spin density is at the central carbon atom, which corresponds to an angle rotation of the benzene rings $\theta \simeq 60°$.[60]

It has been shown[61] that in the radicals (XXVI) and (XXVII) approximately 10% of the spin density is delocalised over remote benzene rings:

$Ph_2\dot{C}-C_6H_4-C\equiv CPh$ (XXVI) $\quad (Ph-C\equiv C-C_6H_4)_3\dot{C}$ (XXVII) .

In broad outline, the distribution of spin density in diarylmethyls differs little from the distribution in triarylmethyls. Table 2 presents the HFC constants and spin densities (ρ_C^π) at the central carbon atom:



The constant for hyperfine coupling with the ^{13}C atom in the central position in the $(C_6Cl_5)\dot{C}Cl$ radical is 39 G, which corresponds to $\rho_C^\pi = 0.9$, and the *g*-factor is 2.0055. The angle of rotation θ is 60°.[60]

Comparison of the ESR spectra of various diarylmethyls led Buchanchenko and Vasserman[65] to the conclusion that, in contrast to its substituted derivatives, the hybridisation of the central carbon atom in the diphenylmethyl radical is not sp^2.

IV. METHODS OF SYNTHESIS

The method of synthesising triarylmethyls by the reduction of halogenotriarylmethanes with metals which Gomberg[1] developed still remains important:

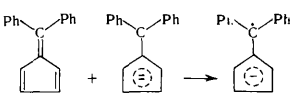
$$Ar_3CX \xrightarrow{M} Ar_3\dot{C} + MX .$$

Silver, mercury, zinc, and various amalgams are most frequently used as reducing agents. Triarylmethyl perchlorates are also employed in place of the halides. The reaction is carried out in an inert medium free from moisture in solvents such as benzene, acetone, ether, petroleum ether, ethyl acetate, and others. In general, triarylmethyl halides and perchlorates are such powerful electron acceptors that they are very readily reduced by a wide range of nucleophilic agents, such as organomagnesium compounds[22, 66], alkoxides and phenoxides[67], sodium diethylphosphite[68], sodium iodide[16], inorganic anions[69], triphenylphosphine and diphenylamine[70], organo-mercury compounds[70], the cyclo-octatetraene dianion[71], and metal ketyls[72].

Diarylmethyls are mainly obtained by Gomberg's method involving the reduction of the corresponding chlorides with metals[64, 73]. Perchlorodiphenylmethyl was obtained for the first time by the reduction of the corresponding chloride with t in (II) chloride[39]:

$$(C_6Cl_5)_2CCl_2 \xrightarrow{SnCl_2} (C_6Cl_5)_2\dot{C}Cl .$$

The diphenylfulvene radical-anion (XIII) was obtained by the reduction of diphenylfulvene by its dianion[21]:



(XIII)

Another general method of synthesising triarylmethyls, involving the reduction of triarylmethyl carbonium ions, was proposed by Conant[74]. Vanadium(II) chloride and sulphate have been used as reducing agents. The carbonium ion was obtained by the dissolution of chlorotriphenylmethane or triphenylmethanol in sulphuric or hydrochloric acid:

$$Ar_3COH \xrightarrow{H^+} Ar_3\overset{+}{C} \xrightarrow{V^{2+}} Ar_3\dot{C} .$$

Chromium[42, 57] and titanium[18] salts have been proposed as reducing agents and trifluoroacetic acid[57] and a mixture of acetic and hydrochloric acids[42] have been suggested as ionising solvents.

The triarylmethyl carbanions formed on dissolution of triarylmethanes in alkalis are readily oxidised to triarylmethyls. The reaction proceeds in an aqueous medium

from which the radical is readily extracted[17]. $KMnO_4$,[17] $K_3Fe(CN)_6$,[28] $AgNO_3$,[8] mercury salts, and bromotriphenylmethane[70] have been used as oxidants:

$$Ar_3CH \xrightarrow{OH^-} Ar_3C^- \xrightarrow{[O]} Ar_3C^{\cdot}$$

Perchlorodiphenylmethyls and perchlorotriphenylmethyls have been obtained by the oxidation of the corresponding carbanions with iodine and oxygen[19].

Zieglar[75, 76] developed a convenient method of synthesising arylalkyl radicals using dibromotetramethylethylene as the electron acceptor:

$$Ar_2RCK + Me_2CBrCBrMe_2 \rightarrow Ar_2RC^{\cdot} + Me_2C{=}CMe_2 + 2KBr$$

Ar_2RCK was obtained by treating the substituted methyl ether with the metal:

$$Ar_2RCOMe + 2K \rightarrow Ar_2RCK + MeOK$$

A modification of Gomberg's method has been proposed by Schmidlin[77], who obtained triphenylmethyl by treating triphenylacetyl chloride with silver:

$$Ph_3CCOCl \xrightarrow{Ag} Ph_3C^{\cdot} + CO$$

Mention may be made of several other methods of synthesising triarylmethyls but these have no preparative value.

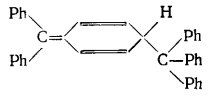
Triphenylmethyl is formed in the decomposition of azo-compounds containing the triphenylmethyl residue[5, 78], t-butyltriphenyl peracetate[79], and *N*-diphenylmethyl-$\alpha\alpha$-diphenylnitrones[80], in the pyrolysis of trityl ethers[81, 82], and in photochemical[83] and certain other reactions[84-87].

The principal method of synthesising the unstable diphenylmethyl radical is photolysis and thermolysis of various diphenylmethane derivatives[45, 62, 88].

V. CHEMICAL PROPERTIES

1. Dimerisation

Tervalent carbon radicals are in thermodynamic equilibrium with their dimers. Since triphenylmethyl was obtained for the first time in an attempt to synthesise hexaphenylethane, the latter was in fact believed to be a dimer of the radical. However, as early as 1905 Jacobson[89] proposed the cyclohexadiene (XXVIII) structure for the dimer:



(XXVIII)

Gomberg[90] also postulated the possibility of several triphenylmethyl dimerisation pathways. The lack of reliable physical methods for the determination of the structure precluded at the time a final solution of this problem and the controversy concerning the structure of triphenylmethyl dimers led to the belief that the only possible structure is that of hexaphenylethane. However, the finding that the dimerisation of tri-(p-*t*-butylphenyl)methyl[91], di-(2,5-di-t-butylphenyl)methyl[92], and di-*p*-substituted diarylmethyls proceeds with extreme difficulty led to the revision by Lankamp et al. of the hypothesis concerning the structure of triarylmethyl and diarylmethyl dimers[93]. The NMR spectra of the diarylmethyl and triarylmethyl dimers which they investigated are consistent with the cyclohexadiene structure and contradict the polyarylethane structure.

The same workers synthesised true tetra-arylethanes by treating diarylmethanols with an excess of vanadium(II) or chromium(II) ions in an acetone solution of hydrochloric acid. True tetra-arylethanes dissociate to diarylmethyl radicals with difficulty and only at a high temperature and the radicals dimerise to cyclohexadienes and not tetra-arylethanes. The melting points of true tetra-arylethanes are much higher than those of the radical dimers. Subsequently the cyclohexadiene structure of the triphenylmethyl dimers was confirmed yet again by ^1H NMR[94] and ^{13}C NMR[95] spectra.

As frequently happens, the fact established not only failed to put an end to the old problems but actually gave rise to new ones. Firstly, not all the radicals dimerised in the "new" way; for example, 9-phenylfluorenyl (V) associates to an ethane derivative[95] and it is probably necessary to determine the structure of the dimer for each radical †. Secondly, it is not clear, for example, why di-(2-t-butylphenyl)methyl dimerises to a cyclohexadiene, while the 2,4- and 2,5-t-butyl derivatives form ethanes[96]. Thirdly, the entire chemistry of polyarylethanes, on which research has been continued for more than 70 years, was suddenly found to be completely unknown.

Other conditions being equal, two main factors influenced the thermodynamic radical – dimer equilibrium: (1) mesomeric stabilisation of the radical and (2) steric interactions in the dimer which promote dissociation.

Estimates of the relative importance of these factors, based on thermochemical data[97], show that the mesomeric effect is approximately twice as effective in promoting dissociation (50 – 55 kcal mole^{-1}) as the steric effect (17 – 22 kcal mole^{-1}).

The heat of dissociation of the triphenylmethyl dimer determined by ESR is 11 kcal mole^{-1}.[98] The activation energy for dissociation, determined by the reaction of this radical with oxygen, is 19 kcal mole^{-1}.[37, 99] A comparison of the thermodynamic data for the recombination and dissociation of diarylmethyls and triarylmethyls has been carried out[37]. While the heats of dissociation of the dimers are almost independent of the solvent, the dissociation constants vary extremely markedly (Table 3).

Table 3. The constants and heats of dissociation of the triphenylmethyl dimer[100]

Solvent	Dissociation constant 10^4K at 20°C	Heat of dissociation, kcal mole^{-1}	Solvent	Dissociation constant 10^4K at 20°C	Heat of dissociation, kcal mole^{-1}
			Ethylene dibromide	3.9	11.4
Propiononitrile	1.2	11.4	Benzene	4.1	11.3
Ethyl benzoate	1.67	12.0	Chloroform	6.9	10.5
Acetophenone	1.70	11.5	Carbon disulphide	19.2	11.0
Dioxan	2.5	11.6			
Bromobenzene	3.7	11.5			

According to Walter's classification[101], triarylmethyl radicals belong to class S, i.e. the degree of dissociation of their dimers increases following the introduction of both electron-donating and electron-accepting substituents.

† A communication was published recently where the literature data on the thermodynamic radical – dimer equilibrium were re-examined in connection with a revision of the structure of the dimers and a correlation equation was successfully applied to the dissociation of the dimers using Taff's steric constants[150].

p-Nitro- and *p*-phenyl substituents have a very marked influence on the dissociation of the dimers (Table 4).

It has been noted that *p*-alkyl-substituted triarylmethyls do not dimerise even at a low temperature. This confirms the cyclohexadiene structure of the dimer. Alkyl substituents in the *meta*- and *para*-positions increase the degree of dissociation but *ortho*-substituents have a particularly marked influence[104]. Thus tri-(2,6-dimethoxyphenyl)-methyl does not dimerise even in the solid state[13]. Coeranthryl (XXV) is also completely dissociated[42]. In contrast, sesquixanthydryl (IX) exists almost entirely as the dimer[13]. This is probably related to the absence of steric hindrance to dimerisation.

Table 4. Dissociation of triarylmethyl dimers[102]

Radical formed	Percentage dissociation in benzene at 5°C	Radical formed	Percentage dissociation in benzene at 5°C
$(C_6H_5)_3\dot{C}$	2—3	$(C_6H_5)_2C{=}CH(C_6H_5)_2\dot{C}$	80
$p\text{-}C_6H_5C_6H_4(C_6H_5)_2\dot{C}$	15	$(CH_3)_3C\,(p\text{-}C_6H_5C_6H_4)_2\dot{C}$	74
$(p\text{-}C_6H_5C_6H_4)_2(C_6H_5)\dot{C}$	79	$\alpha\text{-}C_{10}H_7(C_6H_5)_2\dot{C}$	60
$(p\text{-}C_6H_5C_6H_4)_3\dot{C}$	100	$\beta\text{-}C_{10}H_7(C_6H_5)_2\dot{C}$	33
$(C_6H_5)_3C(C_6H_5)_2\dot{C}$	100	$(\beta\text{-}C_{10}H_7)_3\dot{C}$	24
$(p\text{-}NO_2C_6H_4)_3\dot{C}$	100		

Bisbiphenyleneallyl radicals (XVII) are highly dissociated in solution, although in the solid state they exist mainly as the dimers[27].

Fluorinated triarylmethyls are dissociated in the solid state to the extent of 80 – 90%.[16] Perchlorotriarylmethyls are entirely monomeric both in solution and in the solid state[19].

Table 5. Heats and degrees of dissociation of diarylmethyl dimers[105]

Diarylmethyl dimer	Degree of dissociation, %	Heat of dissociation, kcal mole^{-1}
Di-(2,6-dimethylphenyl) methyl	0.35	22
Di(2-t-butylphenyl)-methyl	0.61	19.7
Di-(2,6-Diethylphenyl)-methyl	1.97	12.0
Triphenylmethyl	12.0	10.9
Di-(2,6-di-isopropyl-phenyl)methyl	100	*

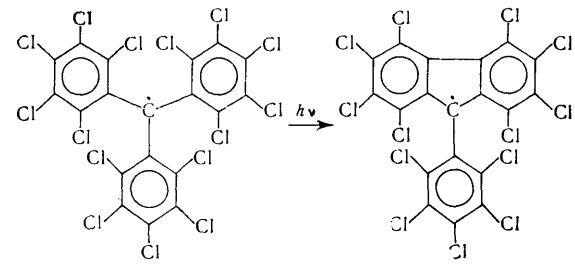
* Not determined owing to the superposition of the disproportionation process

Diarylmethyl radicals dimerise like triarylmethyls, but their dimers are dissociated to a much smaller extent. Diphenylmethyl itself cannot be obtained by the homolytic decomposition of the dimer. Table 5 lists the heats and degrees of dissociation of diarylmethyl dimers in *m*-xylene at 25 °C determined by ESR.

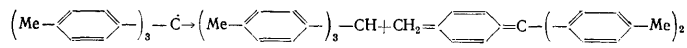
The introduction of alkyl substituents in the *meta*- and *para*-positions does not lead to the dissociation of the dimer. Only the presence of two *ortho*-substituents such as methyl, ethyl, and isopropyl or a single *ortho*-substituent such as t-butyl leads to the dissociation of the dimer. The bis-(2,5-di-t-butylphenyl)methyl dimer dissociates almost completely in solution[64, 96]. Perchlorodiphenylmethyl is the only example of a radical of this type which is fully monomeric even in the crystalline state[39].

2. Disproportionation

Triphenylmethyl solutions in non-polar solvents are decolorised rapidly on standing in the light with formation of triphenylmethane[106] and 1,2-diphenylbisbiphenylenethane[107], i.e. 9-phenylfluorenyl, which is associated more than triphenylmethyl, is formed as an intermediate. Solutions of triphenylmethyl in an ionising solvent such as sulphur dioxide are photochemically stable[108]. The photochemical reaction of perchlorotriphenylmethyl takes place similarly[109]:



p-Alkyl substituents increase the tendency of triarylmethyls towards disproportionation to such an extent that the radical decomposes spontaneously, immediately after formation, into the corresponding triarylmethane and a quinonoid compound which polymerises rapidly[104]:



Di-*p*-t-butyldiphenylmethyl constitutes an exception. It cannot form the quinonoid species by loss of hydrogen. Alkyl substituents in the *meta*- and *ortho*-positions increase the stability of triarylmethyls. Radicals of the allyl type are stable even on heating[27].

In the series of diarylmethyls, 2,4,6,-trialkyl- and 2,5-di-t-butyl-substituted derivatives disproportionate rapidly[36, 91]. The reaction products have not been investigated.

Diarylalkylmethyls disproportionate spontaneously[10] via the reaction

$$2Ar_2\dot{C}Me \rightarrow Ar_2C{=}CH_2 + Ar_2CH{-}Me\,.$$

3. Oxidation and Reduction

Diarylmethyls and triarylmethyls are readily reduced to the corresponding hydrocarbon by sodium amalgam[27], zinc in hydrochloric acid[28], phenylhydrazine[64], and catalytically by activated hydrogen[16]. Bisbiphenyleneallyls are not reduced by reductants such as hydroquinone, sulphite, and ascorbic acid[28].

Alkali metals add reversibly to triphenylmethyl with formation of brick-red salts[111]. Bent et al.[112] used this reaction to determine the electron affinity of triphenylmethyl and found it to be 17.9 kcal mole^{-1}.

Inert perchloro-radicals are reduced by potassium in ether to the corresponding carbanions[19]. Triphenylmethyl can also be reduced by a mixture of magnesium and magnesium bromide with formation of an organomagnesium compound[113].

Iron(III), mercury(II), silver(I), and gold(III) salts readily oxidised triphenylmethyl. In the $SO_2 - O_2$ system triphenylmethyl is oxidised to the carbonium ion[114], while at a rotating platinum electrode perchlorotriphenylmethyl can be reversibly reduced and oxidised to the corresponding ion[115].

4. Reaction with Radicals

Almost all tervalent carbon radicals interact with oxygen forming the colourless peroxide $Ar_3COOCAr_3$. The qualitative detection of triarylmethyls, the so called Schmidlin test[116], depends on this reaction. The coloured solution of the radicals is decolourised on shaking in air but subsequently the colour returns as a result of the dissociation of the dimer. The Schmidlin test can be repeated several times until the quantitative formation of the peroxide takes place. Janzen et al.[117] showed by ESR that the first stage in this reaction is the reversible formation of the peroxy-radical:

$$Ph_3\dot{C} + O_2 \rightleftarrows Ph_3C\dot{O}O \ .$$

Bisbiphenyleneallyls (XVIII, R = Ar) are stable in relation to oxygen[25]. Triarylmethyls combine with nitric oxide[118] forming hyponitrites; it has been suggested that this reaction proceeds via a stage involving the formation of nitrones[119].

The peroxide formed when oxygen acts on diarylmethyls is unstable and decomposes with formation of Ar_2CO, Ar_2CHOH, and $Ar_2CHOCHAr_2$.[120] The same products are formed when diarylmethyls react with NO.

The reactions of diaryl- and triarylmethyls with O_2 and NO have been frequently used to obtain thermodynamic data for the dissociation of radical dimers.

Nitrogen dioxide reacts with triphenylmethyl both via the nitrogen and via the oxygen with formation of two products – nitrotriphenylmethane and triphenylmethyl nitrite[118]:

$$Ph_3\dot{C} + O{=}N{-}\dot{O} \leftrightarrow O{=}\overset{+}{N}{-}O^- \rightarrow Ph_3C{-}N\begin{matrix}O\\ \diagup\!\diagdown\\ O\end{matrix} + Ph_3C{-}O{-}N{=}O \ .$$

On heating, triarylmethyls can abstract hydrogen from certain hydrocarbons, for example from toluene with formation of triarylmethane and triarylbenzylmethane via the mechanism[121]:

$$Ar_3\dot{C} + PhCH_3 \rightarrow Ar_3CH + Ph\dot{C}H_2 \ ,$$

$$Ar_3\dot{C} + Ph\dot{C}H_2 \rightarrow Ar_3CCH_2Ph \ .$$

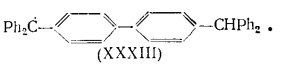
Active radicals interact with triarylmethyls, adding to the *p*-position of the benzene ring[83]:

$$Ph_3\dot{C} + \dot{P}h \rightarrow \begin{matrix}Ph\\ \diagup\\ H\end{matrix}\!\!\!

Compounds of this type can exist both in the triplet biradical form (a) and in the singlet quinonoid form (b). The amount of the biradical form depends on the energy difference between the singlet and triplet levels. For Thiele's hydrocarbon[134] (XXXII, $n = 1$), this energy difference is high (5.3 kcal)[135], as a result of which the compound is diamagnetic[136].

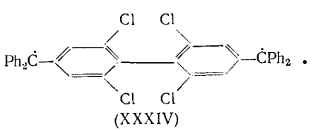
The situation is more complicated with Chichibabin's hydrocarbon[137] (XXXII, $n = 2$). The excitation energy for this compound is 2.5 kcal, i.e. even at room temperature there is a possibility of a thermodynamic equilibrium involving a small amount (1 – 3%) of paramagnetic species. Such a small admixture of paramagnetic species cannot be detected by magnetic methods[138], but has been detected by ESR.[136] However, a new problem arises, which enabled McConnell to formulate the so-called "biradical paradox"[139]. The point is that theory predicts $J = 15 \times 10^6$ MHz for electron – electron interaction in biradicals of the type of Chichibabin's hydrocarbon, while the experimental value is only 70 MHz. The problem was solved by analysing the ENDOR spectra[140].

It was found that the ESR spectra of solutions of Chichibabin's hydrocarbon are due to the presence of the monoradical (XXXIII), which is formed from (XXXII, $n = 2$) following the abstraction of a hydrogen atom from the solvent:



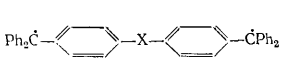
(XXXIII)

The breakdown of the coplanarity of the benzene rings due to the presence of *ortho*-substituents can stabilise the biradical form[141, 142]. Although (XXXIV) does give an ESR spectrum in the solid state, it too is not a biradical[143]:



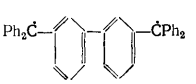
(XXXIV)

The introduction of non-conducting bridges such as O and CH_2 makes it possible to obtain stable hydrocarbon biradicals (XXXV)[136]:



X=O, $(CH_2)_n$

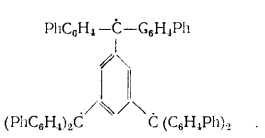
(XXXV)



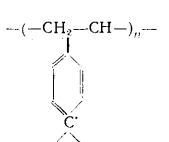
(XXXVI)

Schlenk's hydrocarbon (XXXVI), which is incapable of giving rise to quinonoid forms, also has a triplet ground state[144]. In solution (XXXVI) is largely associated[145] and its ESR spectrum is additionally complicated by the presence of monoradicals[146].

Triradicals (XXXVII)[147] and polyradicals (XXXVIII)[148] of the triarylmethyl series were obtained. In solution these radicals are probably associated:

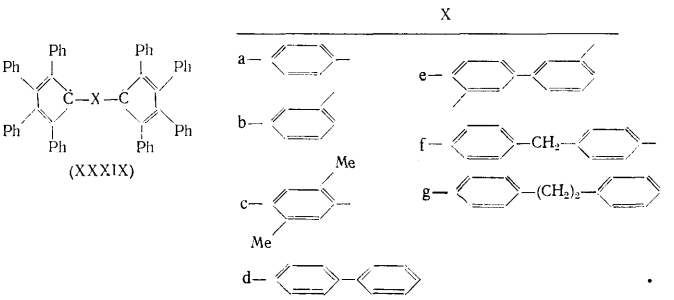


(XXXVII)



(XXXVIII)

In contrast to the compounds described above, the biradicals (XXXIX, $a-g$ are not associated[149]. All these, with the exception of (XXXIXa), have a triplet ground state; although (XXXIXa) is in fact paramagnetic, it is not a biradical:



(XXXIX)

The chemical properties of biradicals and polyradicals differ little from those of the monoradicals.

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Institute of Chemical Physics,
USSR Academy of Sciences,
Moscow

U.D.C. 547.914.3

Non-equilibrium Copolycondensation in Homogeneous Systems

V.A.Vasnev and S.I.Kuchanov

Theoretical and experimental data for the composition and structure (microheterogeneity) of copolymers obtained by non-equilibrium copolycondensation in homogeneous systems are considered. The effect of the relative reactivities of the comonomers, the reactivities of the first and second groups of the intermonomer, the order and duration of addition of the initial compounds to the reaction zone, and other factors on the composition and microheterogeneity of the copolymers has been demonstrated in relation to interbipolycondensation. The available experimental literature data have been compared with the results of calculations based on a quantitative theory of homogeneous copolycondensation.
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I. INTRODUCTION

Copolycondensation embraces the polycondensation of three and more monomers when none can condense independently under the conditions of the given process. When such condensation is possible, for example, when hydroxy- or amino-acids are employed as the monomers, copolycondensation includes also processes involving two monomers. Since the chains of polycondensation copolymers contain two or more types of units, they will differ from one another by their composition and structure (microheterogeneity) as well as the degree of polymerisation. An important task in the study of copolycondensation (and incidentally in copolymerisation in general) is the determination of quantitative relations between the reactivities of the monomers and the process conditions on the one hand and the characteristics of the polymer obtained as the product on the other. However, whereas for radical polymerisation this has been largely achieved as early as 20 years ago[1,2], systematic studies on copolycondensation on these lines were begun only in the very recent years.

Possibly this is because in the early stages of the investigation of polycondensation mainly equilibrium processes were studied. The synthesis of high-molecular-weight products by this method is known[3,4] to require, firstly, an equimolar mixture of monomers and, secondly, the reaction must be continued up to conversions close to 100%. In this method of copolycondensation the entire initial monomer is present in the polymer chains at the end of the reaction and hence the problem of composition does not arise. The inhomogeneity of the composition of the copolymer should not be unduly great, because the distribution of the equilibrium copolycondensation products with respect to composition should be very narrow. This factor, which makes it possible to assume with a high degree of accuracy that all the macromolecules have the same chemical composition, is specific to equilibrium copolycondensation and generally speaking does not apply to copolymerisation. In the latter process the possibility of appreciable inhomogeneity in composition arises because a copolymer appreciably enriched in one of the monomers can be formed in the early stages, while in subsequent stages it may be enriched in the other monomer. In equilibrium copolycondensation the vigorous occurrence of exchange reactions "mixes" the compositions of the individual macromolecules, eliminating thereby the above cause of inhomogeneity of the composition and leading to a random (statistical) distribution of units in the copolymer chains. Consequently, equilibrium copolycondensation results in the formation of macromolecules with a statistical distribution of units which have virtually identical compositions corresponding to that of the initial monomeric mixture. Hence it is clear that in equilibrium copolycondensation there is no need to determine the dependence of the statistical characteristics of the copolymer on the process conditions. This problem does however become very urgent for non-equilibrium copolycondensation, which is characterised by the absence of exchange and degradative reactions[5]. In this case the difference between the homophase and heterophase methods of carrying out the process, the chemical reactions of which may be complicated by the effects of diffusion and adsorption of the reactants on the interface, is shown particularly clearly. In conformity with the title of the review, we shall consider only processes involved in homogeneous copolycondensation; these are the simplest and most systematically investigated both theoretically and experimentally. Naturally any quantitative description of the macrokinetics of heterophase copolycondensation is impossible without a preliminary determination of the general characteristics of homogeneous processes.

The review does not deal with processes associated with the molecular weight distribution and with the molecular weights of polycondensation copolymers. This is because, on the one hand, there are at present no reliable experimental data whereby an unambiguous quantitative relation can be established between the above parameters and the reactivities of the initial compounds and conditions under

which they are injected. On the other hand, since the chain termination rate constants are unknown, it is impossible to compare the theoretical molecular-weight distributions and molecular weights with the observed values. The range of problems considered in the present review (chemical composition and structure of the chains in the copolymer macromolecules) is independent of side reaction leading to chain termination and the above characteristics of copolymers are determined only by the relations between the chain propagation rate constants.

In connection with the development of new methods for the investigation of high-molecular-weight compounds and in particular the considerable progress achieved in the application of high-resolution nuclear magnetic resonance (NMR), it has become possible to obtain reliable quantitative data for the compositions and structures of copolycondensation products.

The high accuracy of this method makes it possible, when the appropriate theory is available, to discover detailed features of the kinetics of the formation of copolymer chains. The fruitful application of high-resolution NMR to the study of products of homogeneous copolycondensation made it possible, despite the relatively small number of studies in this field, to establish the general characteristics of the process and has greatly stimulated the development of its quantitative theory.

II. CLASSIFICATION OF PROCESSES IN HOMOGENEOUS NON-EQUILIBRIUM COPOLYCONDENSATION AND METHODS OF QUANTITATIVE DESCRIPTION OF THE COPOLYMERS

Linear copolycondensation of compounds containing not more than two functional groups has been investigated theoretically and experimentally to the greatest extent. The simplest instances of linear copolycondensation, which at the same time exhibit all the characteristic features, are bipolycondensation and interbipolycondensation. The first case, where at least one of the two initial compounds employed in the reaction is capable of self-condensation under the conditions of the given processes, can be achieved, for example, with monomers of the amino- or hydroxy-acid type. The second case, where three monomers A–R–A, B–S–B, and C–I–C are involved in the reaction, is more common. The first two, called the comonomers, do not react directly with one another, but each condenses with the third component (the intermonomer).

The interbipolycondensation products can be divided into copolymers belonging to one or different classes. The former are formed from comonomers with identical functional groups. An example of such copolymers is provided by mixed polyamides synthesised from two diamines and one dicarboxylic acid chloride or from one diamine and two dicarboxylic acid chlorides. In order to synthesise copolymers of the second group, it is necessary to employ comonomers with different functional groups. Polyamidoesters obtained by the copolycondensation of a diamine and a glycol with a dicarboxylic acid, may serve as an example of such copolymers.

The chains formed in the course of interbipolycondensation have the structure...–IRIRISIRI–..., in which the comonomer units alternate with the intermonomer units. In order to characterise the composition of the copolymer, it is sufficient to indicate the fraction of units of one of the comonomers, P_R or P_S, while the fraction of the second is determined from the self-evident equality $P_R + P_S = 1$.

In order to describe the inhomogeneity of the composition of the copolycondensation products, one can introduce a distribution function for the macromolecules with respect to size (the number of polymer units) and composition. By analogy with the molecular weight distributions (MWD), this function is known as the size–composition distribution (SCD).

The simplest unit suitable for the description of the chain structure (microheterogeneity) of copolymers is a triad. Homotriads (RIR and SIS) and heterotriads (RIS) are distinguished. In the simplest description of the nature of the distribution of the units R and S in the copolymer chain, one can specify the fractions of the P_{RR}, P_{SS}, and P_{RS} triads of various types. The inhomogeneity of the interbipolycondensation products is estimated quantitatively in terms of the microheterogeneity coefficient K_M, which is expressed in terms of the fractions of various triads by means of the relation

$$K_M = \frac{P_{RS}}{P_{RS} + 2P_{RR}} + \frac{P_{RS}}{P_{RS} + 2P_{SS}} . \qquad (1)$$

For a mixture of two homopolymers, $P_{RS} = 0$ and correspondingly $K_M = 0$, while for a copolymer with a regular alternation $P_{RR} = P_{RS} = 0$, which corresponds to $K_M = 2$. Between these two extreme cases, corresponding to fully ordered arrangement of units in macromolecules, there are all possible values of the microheterogeneity coefficient, $K_M = 1$ corresponding to a statistical (i.e. the most disordered) distribution. Consequently the absolute deviations of K_M from unity can be used for a quantitative assessment of the degree of order in the distribution of units in the copolymer and from the latter one can infer the direction of the deviation—the tendency of the monomer residues towards a regular alternation in the chains ($K_M > 1$) or (when $K_M < 1$) towards the formation of long blocks of both comonomers. It has been shown [6] that the composition and the average block lengths L_R and L_S of a copolymer with a fairly high molecular weight most molecules of which consist of numerous blocks, can be determined with the aid of the relations

$$P_R = P_{RR} + \frac{P_{RS}}{2}, \; P_S = P_{SS} + \frac{P_{RS}}{2}, \; L_R = \frac{2P_R}{P_{RS}}, \; L_S = \frac{2P_S}{P_{RS}} \qquad (2)$$

in terms of the fractions of various triads. In this case Eqn. (1) assumes a particularly clear form:

$$K_M = \frac{1}{L_R} + \frac{1}{L_S} . \qquad (3)$$

Another more detailed method of describing the microheterogeneity of copolycondensation products, which however is more difficult to test experimentally, consists in finding the distribution functions for blocks of various comonomer units with respect to their lengths.

III. INITIAL COMPOUNDS

1. Reactivity of Bifunctional Monomers

The view according to which one of the main factors influencing the composition and structure of copolymers obtained by non-equilibrium polycondensation is the relative reactivity of the comonomers is widely held at present [7,8]. Evidently, this question is closely related to the problem of the constancy of the reactivity of the functional groups of polyfunctional monomers. This type of constancy is as a rule postulated in a theoretical examination of various aspects of polycondensation processes [9].

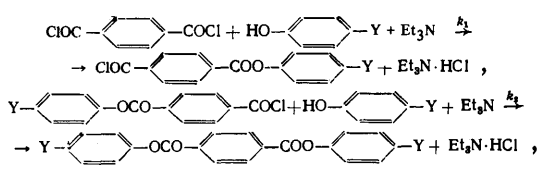
However, there is at present no doubt that the reactivity of the functional groups of many monomers changes in the course of the process[4,5].

Comparatively recently a number of studies were published in which the reactivity of certain initial aromatic compounds widely used in non-equilibrium polycondensation was estimated from the p-electron density at the corresponding atom of the functional group: the nitrogen atom of the NH_2 group in diamines and tetramines[10,11], at the oxygen atom of the OH group in bisphenols[12], and at the carbon atom of the COCl group in dicarboxylic acid chlorides[13].

A preliminary conclusion concerning the reactivity of dicarboxylic acid chlorides was reached with the aid of nuclear quadrupole resonance (NQR) spectra. It has been established that the frequency of the chlorine atom in COCl depends on the electron density in the carbonyl group[14]. A convenient criterion of the capacity of the bisphenol and diamines components for involvement in the polycondensation process is provided by the acid–base properties of their functional groups: phenolic[15,16] or amino-groups[17,18]. Sokolova and Sokolov[19] suggest that the thermochemical method be employed for rapid estimation of the reactivity of the dicarboxylic acid chloride, the principle of which consists in the determination of the heats of reaction of the given monomer with solvents.

Special evidence is not required to show that the methods discussed above can yield only a preliminary fairly qualitative idea about the reactivity of the monomer. Thus, on the one hand, the change in any one characteristic, for example the pK for the acid dissociation of bisphenols, can in some cases entail an increase of the reactivity of the monomers and a decrease in others[15]. On the other hand, it is known that the variable influence of polar effects on the reactivity of a particular functional group depends significantly on various factors: the type of reaction, its mechanism, the nature of the solvent, temperature, etc.[20]

A more effective method for the solution of the above problems is based on kinetic studies of the reactions of bifunctional monomers with monofunctional compounds, which are carried out under conditions close to those in polycondensation. An example of such a reaction is provided by the acylation of phenols by terephthaloyl chloride in the presence of triethylamine (Table 1):



which simulates acceptor–catalytic polyesterification:

$$ClOC-Y'-COCl+HO-Y''-OH+2Et_3N \rightarrow \cdots-CO-Y'-COO-Y''-O-\cdots+2Et_3N\cdot HCl.$$

The data presented in Table 1 show that the rate constant ratio for the first and second COCl groups is not constant and depends on the structure of the phenol. As shown recently,[21] it is important to note that the reactivity of the second group of the bifunctional monomer relative to the first may not only decrease (Table 1, Nos. 1–3) but also increase (Table 1, No. 4).

Kuritsyn and Kuritsyna[22], Sokolov and Kuritsyn[23], and Vorob'ev et al.[24] reported the results of kinetic studies on the reaction of carboxylic acid chlorides with aniline and its derivatives (Table 2). They observed that the ratio of the reactivities of the first and second acid chloride groups depends significantly on the nature of the aromatic amine.

The reactivity of the first COCl group of terephthaloyl chloride (Table 2) in the reaction with aniline (in benzene at 25°C) is higher than that of the first COCl group in isophthalic and carborane-m-dicarboxylic acid chlorides by factors of 1.6 and 2.7 respectively.

Table 1. The results of a kinetic study of the reaction of terephthaloyl chloride with phenols in the presence of triethylamine in dioxan at 30°C[21].

No.	Y in 	$2k^1$	k^2	$\varkappa=\frac{k^1}{k^2}$	No.	Y in 	$2k^1$	k^2	$\varkappa=\frac{k^1}{k^2}$
		litre^2 m^{-2} s^{-1}					litre^2 m^{-2} s^{-1}		
1	CH_3	23±2	4.7±0.3	2.46	3	Cl	34±2	15±1	1.12
2	H	20±1	6.8±0.8	1.49	4	NO_2	96±5	62±3	0.78

A kinetic study of the reaction of bisphenols with substituted benzoic acid chlorides in the presence of triethylamine established that the reactivities of the first and second phenolic groups of 2,2-di-(4-hydroxyphenyl)propane and di-(4-hydroxyphenyl) ether are the same (Table 3).[25]

Table 2. The rate constants for the reactions of dicarboxylic acid chlorides with aromatic amines in benzene at 25°C.

Aromatic amine	$k^1\cdot10^2$	$k^2\cdot10^2$	k^1/k^2
	litre mole^{-1} s^{-1}		
Isophthaloyl chloride (Refs.22 and 23)			
m-Chloroaniline	3.9	2.5	1.5
p-Chloroaniline	14.6	9.4	1.5
Aniline	49.6	2.9	1.7
m-Toluidine	98.0	4.9	2.0
Terephthaloyl chloride (Refs.22 and 23)			
m-Chloroaniline	4.51	1.6	2.7
p-Chloroaniline	18.6	5.0	3.7
Aniline	80.9	19	4.2
m-Toluidine	138	30	4.6
p-Toluidine	220	45	4.9
Carborane-*m*-dicarboxylic acid chloride (Ref.24)			
Aniline	29.9	16.2	1.8
Benzophenone-4,4′-dicarboxylic acid chloride (Refs.22 and 23)			
m-Chloroaniline	8.56*	51*	1.7
Naphthalene-2,6-dicarboxylic acid chloride (Refs.22 and 23)			
m-Chloroaniline	2.45	1.5	1.6

*At 45°C.

The problem of the effect of the length of the macromolecule on the reactivity of its terminal groups is undoubtedly of independent interest. Until recently, studies on these lines have hardly been made. Recently, Turska and coworkers[26] established that the rate constant for non-equilibrium polyesterification in solution is influenced by the solvent power of the organic medium. The explanation is that the reactivity of the terminal groups of the macromolecule depends on chain length.

A number of studies have been published lately in which the relative reactivities of the comonomers (diols) in the interaction with the intermonomer (terephthaloyl chloride) were estimated from the contents of the comonomer residues in the polymeric product (Table 4).[27-29]

Table 3. The results of kinetic studies of the reaction of bisphenols with substituted benzoyl chlorides in the presence of triethylamine in dioxan at 30°C.[25]

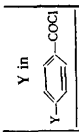
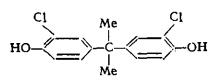
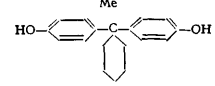
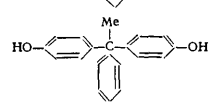
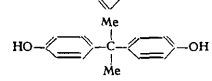
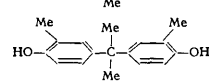
Y in 	$2k^1$	k^2	k^1/k^2
	litre^2 mole^{-2} s^{-1}		
Hydroquinone			
H	0.80±0.08	0.34±0.04	1.18
NO_2	48±5	21±1	1.13
2,2-Di-(4-hydroxyphenyl)propane			
H	0.52±0.06	0.26±0.04	1.00
NO_2	38±2	18±1	1.04
Di-(4-hydroxyphenyl)ether			
Me	0.44±0.04	0.21±0.02	1.03
H	0.86±0.09	0.40±0.03	1.07
Cl	3.1±0.3	1.5±0.1	1.01
NO_2	73±5	37±2	0.99

Table 4. The results of the determination of the relative reactivities of diols in polycondensation with terephthaloyl chloride in the presence of a tertiary amine in dichloroethane at 40°C.[27,28]*

Reference diol: formula	pK_{A_1} in dimethyl sulphoxide at 25°C (Ref.15)	Copolycondensation constants r': pyridine	triethylamine
	12.5	(1.00)	(1.00)
	13.0	0.64	0.40
	13.0	0.50	0.40
	13.1	0.59	0.30
	13.1	0.19	0.16
$HO(CH_2)_6OH$	15.1**	1.20	0.03
H_2O	15.7**	—	0.02

*The molar ratios of the diols, terephthaloyl chloride, and triethylamine were 1 : 1 : 1 : 2 and those of the diols, terephthaloyl chloride, and pyridine were 1 : 1 : 1 : 6.
**pK_{A_1} in water.

2. The Order of Introduction of the Initial Compounds into the Reaction Zone

In the synthesis of copolymers by non-equilibrium copolycondensation several methods for the introduction of the initial compounds into the reaction zone are employed. Single-stage copolycondensation is frequently carried out in such a way that all the initial compounds are present in the reaction zone from the very beginning of the process. This order of introduction of the monomers is most frequently employed in the synthesis of copolymers by both non-equilibrium and equilibrium copolycondensation[3-5]. In two-stage copolycondensation the initial compounds (these are usually the comonomers) are introduced into the reaction zone in succession at specified time intervals.

One of the ways of carrying out the process involves three-stage copolycondensation which some investigators employ for the synthesis of block copolymers[30,31]. In this procedure each comonomer is subjected initially to polycondensation with the intermonomer in different reaction vessels. In one system the intermonomer is present in an excess and in the other in a deficiency, but the overall molar amounts of the interacting functional groups are as a rule equal in both vessels. At the end of the polycondensation the systems are combined, which results in copolycondensation between the intermediates formed.

In the synthesis of copolymers by non-equilibrium polycondensation a gradual introduction of one of the initial compounds, usually the intermonomer, into the reaction zone has begun to be used recently[29,32]. This order of addition of the initial compounds frequently leads to the formation of block copolymers.

IV. THEORY OF NON-EQUILIBRIUM COPOLYCONDENSATION IN HOMOGENEOUS SYSTEMS

1. Composition of the Copolymers and Its Inhomogeneity

The task of the theory of copolycondensation is to establish quantitative relations between the average composition of the copolymer, the inhomogeneity of its composition, and the structure of its chains on the one hand and the proportions and reactivities of the initial compounds and the method of their introduction into the reaction zone on the other. As stated above, for equilibrium copolycondensation this task is trivial but for the non-equilibrium processes discussed in this review it becomes important.

It is noteworthy that a similar problem arises also in radical copolymerisation and considerable advances have been made in its solution[1,2]. However, the processes discussed in this review have many important characteristics which distinguish them from copolymerisation and therefore require separate analysis. The first of these differences is a qualitatively different mechanism of polymer chain propagation, which generally speaking makes it impossible to regard chain propagation in copolycondensation as the usual Markov process[1,2]. Another important difference is in the time scales of the formation of polymer chains in the two processes. In radical copolymerisation the chain-formation time, which is comparable to the lifetime of the radical, usually constitutes a negligible proportion of the duration of the process itself. The latter factor, which makes it possible to regard the conditions governing the formation of each individual chain as unaltered, does not hold in copolycondensation where the time required for the formation of high-molecular-weight products is comparable to the duration of the process. The third characteristic feature of copolycondensation kinetics is the possibility of the interdependence of the reactivities of the functional groups of the initial monomers. As will be shown below, this phenomenon plays the leading role in the formation of the copolymer chain microstructure.

At present the number of computational theoretical studies described in the literature and dealing with homogeneous copolycondensation is extremely small. The first classification of these processes was made by Shtraikhman[33], who also derived an equation for the composition of the interbipolycondensation products when all the initial compounds are introduced simultaneously into the reaction zone. The composition of the copolymer is then defined thus:

$$P_R = \frac{[A]_0 - [A]}{[A]_0 - [A] + [B]_0 - [B]}; \quad P_S = \frac{[B]_0 - [B]}{[A]_0 - [A] + [B]_0 - [B]}, \qquad (4)$$

where the variation of the concentrations of the functional groups of the comonomers [A] and [B] with their initial values $[A]_0$ and $[B]_0$, the reactivities, and the degree of reaction is found by solving differential equations describing the process kinetics. From these equations for the case of the unaltered reactivities of all the functional groups A, B and C, Shtraikhman[33] and, independently, Beste[34] obtained the relations

$$\frac{[A]}{[A]_0} = \left(\frac{[B]}{[B]_0}\right)^r, \quad [A] + [B] = [A]_0 + [B]_0 - [C]_0 p, \qquad (5)$$

where $p = \{[C]_0[C]\}/[C]_0$ is the conversion, [C] and $[C]_0$ are the current and initial concentrations of the functional groups of the intermonomer C–I–C, and r is its relative reactivity in condensation reactions with the comonomers A–R–A and B–S–B. The variation of the composition of the products with conversion has been investigated[35] on the basis of Eqns. (4) and (5) for different values of the parameter r and different proportions of the monomers. For initial compounds with interdependent functional groups, it is impossible to obtain mathematical formulae analogous to Eqn. (5) and the composition of the copolymer was calculated for individual specific instances on a computer[36]. However, it is noteworthy that the problem of the determination of the composition of the non-equilibrium homogeneous interbipolycondensation products with simultaneous introduction of all the initial compounds arises only when they are present in non-equimolar proportions whereupon the final reaction products are oligomers with a small number of units. In order to obtain high-molecular-weight products in this process, it is necessary (as in equilibrium copolycondensation) to carry out the reaction between rigorously equimolar amounts of the monomers until a high conversion approaching 100% is reached. With this method of simultaneous introduction of the starting materials, the composition of the copolymer is always the same as that of the initial monomer mixture and the problem of its calculation does not arise.

Another situation obtains when any one of the initial compounds is gradually introduced into the reaction zone, which may lead to the formation of high-molecular-weight products even when the initial molar ratios of the monomers deviate appreciably from unity[37,38]. For this purpose, it has been necessary to introduce the monomer in excess into the reaction zone at a rate many times less than the rate of its chemical interaction. A typical example of a process of this kind is provided by interbipolycondensation with gradual introduction of the intermonomer into the reaction zone. When all the functional groups of the monomers are independent, the Shtraikhman–Beste equation [Eqn. (5)] is again valid for this process. However, when the intermonomer is introduced fairly slowly, high-molecular-weight products can be formed long before the reaction of the two monomers. This happens when the reactivity of one of the comonomers greatly exceeds that of the other. The process can then be arbitrarily divided into two stages. At the end of the first stage, which is analogous to the polycondensation of the more reactive comonomer with an excess of the intermonomer, high-molecular-weight products are already formed, although the second comonomer has still hardly reacted. Consequently, in this method of carrying out the process it is possible to obtain a high-molecular-weight polymer the composition of which differs from those of the initial compounds. At the beginning the polymer is enriched in the more reactive comonomer and then, as conversion increases and this monomer is exhausted, the copolymer composition begins to approach that of the monomer mixture. The smaller the difference between the reactivities of the comonomers the less distinct are the two stages of the process and the smaller the molecular weight of the products at intermediate conversions. In the limiting case of equal reactivities of the comonomers high-molecular-weight products are formed only after the complete conversion of both comonomers.

It is noteworthy that theoretically only one case is possible in the synthesis of high-molecular-weight products in homogeneous irreversible polycondensation with simultaneous introduction of a non-stoichiometric mixture of the initial compounds[39]. For this, it is necessary that, following the reaction of the first functional group of the monomer taken in excess, the reactivity of the second group should increase sharply. If it were possible to select such an intermonomer, then, in the course of its homogeneous irreversible interbipolycondensation with a mixture of two comonomers having markedly different reactivities, the composition of the resulting copolymer would differ from those of the initial compounds even when the latter are introduced simultaneously. However, the above case is hypothetical, since so far monomers in which the reactivity of the second group greatly exceed that of the first have not been found.

For the same average composition of the polymerisation copolymers, their properties may[40] differ considerably depending on the type of distribution of the compositions of the individual macromolecules, i.e. on the inhomogeneity of the composition of the products. Despite its great practical importance, until recently the problem of this type of inhomogeneity of polycondensation copolymers was not investigated. The method of calculations on the kinetics of homogeneous irreversible polycondensation developed by Kuchanov and Pis'men[41,42] makes it possible to calculate the distribution of the macromolecules with respect to size and composition (DSC) in copolycondensation[6]. It is noteworthy that this method is very general, since the calculation based on it does not impose any limitations either on the number of the initial compounds, or on the relative reactivities of their functional groups (they can be interdependent), or on the number of these groups in the monomer molecules. The latter factor permits the calculation of DSC not only of linear but also of branched products. Another general approach to the calculation of DSC, based on methods of the theory of random processes, has been proposed[43]. However, the relations obtained by the authors cannot be used to describe the copolycondensation of monomers with interdependent functional groups. Their results[43] include as a special case the formulae derived by Cito[44] for the products of the interbipolycondensation of a stoichiometric mixture of monomers with the same reactivities.

On the basis of Kuchanov's results[6], it is possible to show that the kinetic calculation of the distribution of the homogeneous irreversible copolycondensation products

with respect to size and composition leads to the important conclusion that there is a virtual absence of inhomogeneity in the composition of polycondensation copolymers. This is valid provided that their average degree of polymerisation is fairly high. This conclusion does not apply to oligomeric products, the length of which is comparable to that of an individual block. On the other hand, if most of the macromolecules consist of many blocks, then calculation shows that all these molecules may be regarded as having identical compositions to a high degree of accuracy. The latter conclusion is diametrically opposed to Turska's view[7], according to which the composition of the above copolymers should not be inhomogeneous. A conclusion of this kind can be reached when the relations governing the formation of chains in radical copolymerisation are extended to copolycondensation processes. However, one then fails to take into account the fact that the time required for the formation of each individual chain constitutes in the first instance a negligible proportion of the duration of the process itself, while in the second instance, is comparable to this duration.

2. Calculation of the Chain Structure of the Copolymers

In devising a quantitative theory of homogeneous copolycondensation, the most complex problem is that of the calculation of quantities characterising the microheterogeneity of the products. An attempt at a quantitative description of the chain structure of polycondensation copolymers was made by Sawada[45,46], who related by a statistical method the microheterogeneity of the copolymer to the changes in the thermodynamic potentials in the course of the chemical reaction. Since his relations[45,46] do not contain kinetic constants explicitly, they do not make it possible to discover the effect of the reactivities of the monomers on the chain structure.

The coefficient of microheterogeneity K_M defined by Eqn. (1) is a simple characteristic of the copolymer chain structure which can be conveniently determined both theoretically and experimentally. Kuchanov's calculation[6] of K_M for interbipolycondensation products with simultaneous introduction of all the monomers shows that the nature of the distribution of units in the chains is determined mainly by the interdependence of the reactivities of the functional groups in the intermonomer. If these groups are independent, then according to theory $K_M = 1$ and the distribution of units is always statistical for any conversion, proportions of the monomers, and their reactivities. This conclusion disproves the view put forward by some investigators[7,35] that the products of non-equilibrium homogeneous copolycondensation have a block structure. In contrast to copolymerisation, a statistical distribution of the chain units of polycondensation copolymers can occur however large the difference between the reactivities of the comonomers. A general correspondence has been established between the functional group reactivity difference in the intermonomer and the distribution of chain units in the copolymer[6]. If following the reaction of the first group of the intermonomer the reactivity of the second group increases, a tendency of the monomer units towards alternation should be observed ($K_M > 1$); in the opposite case an increase of the reactivity of the second group should entail the appearance of a tendency towards the formation of blocks ($K_M < 1$). For the same intermonomer with interdependent reaction centres, the order in the distribution of chain units in the copolymer increases with the difference between the reactivities of the comonomers.

Theoretical study of the dependence of K_M on the method of introduction of the monomer[47] has shown that there is a possibility of obtaining block copolymers in homogeneous non-equilibrium copolycondensation even when an intermonomer with independent functional groups is involved. This case occurs when the intermonomer is introduced fairly slowly into the reaction zone. When the intermonomer is introduced at a rate much lower than that of the condensation reaction, the following expressions are obtained for the average block lengths and K_M:

$$\frac{1}{L_R} = \alpha_S \mathcal{J}, \frac{1}{L_S} = \alpha_R \mathcal{J}, K_M = (\alpha_R + \alpha_S)\mathcal{J} , \quad (6)$$

$$\mathcal{J} = \int_0^1 \frac{r x^{r-1}\, dx}{\alpha_S + \alpha_R x^{r-1}} , \quad (7)$$

which depend only on the mole fractions α_R and α_S of the comonomers and their relative reactivity parameter r, but are independent of the rate of supply of the intermonomer to the reaction zone. The variation of K_M with r for $\alpha_R = \alpha_S$ (Fig. 1) shows that an increase of the difference between the reactivities of the comonomers leads in the present instance to the formation of longer blocks.

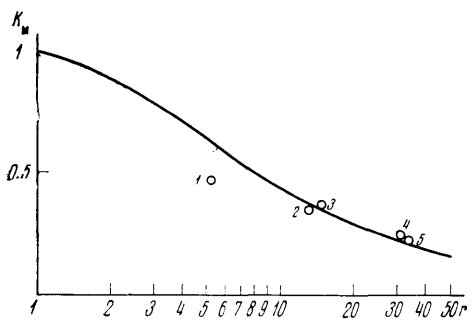


Figure 1. Theoretical variation of the microheterogeneity coefficient with the relative reactivity parameter of the comonomers on slow introduction of the intercomponent (see Table 9 for the significance of the experimental points).

The results obtained by Kuchanov[47] can be used to calculate the K_M for the products of two-stage interbipolycondensation. In this case, apart from its variation with α_R and α_S, K_M depends only on the parameter κ which is equal to the ratio of the reactivities of the first and second groups of the intermonomer in its reaction with the monomer which is introduced first. A plot of K_M against κ for an equimolar ratio of comonomers with independent functional groups is presented in Fig. 2. The same plot evidently describes single-stage copolycondensation with simultaneous introduction of all the initial compounds in the limiting case where the reactivities of the comonomers differ markedly. κ then refers to the reaction of the intermonomer with the more reactive comonomer.

The second method of describing the microheterogeneity of copolymers consists in specifying a distribution function with respect to the block lengths of different monomeric units. A distribution function of this kind was calculated

for the first time by Beste[34] for the products of the interbipolycondensation of a stoichiometric mixture of monomers with independent functional groups. Using a statistical method, he obtained the following expression for the fractions of the comonomer units entering into a block with a length n:

$$W_R(n) = (1 - \nu_{RR})^2 n \nu_{RR}^{n-1}, \; W_S(n) = (1 - \nu_{SS})^2 n \nu_{SS}^{n-1} . \quad (8)$$

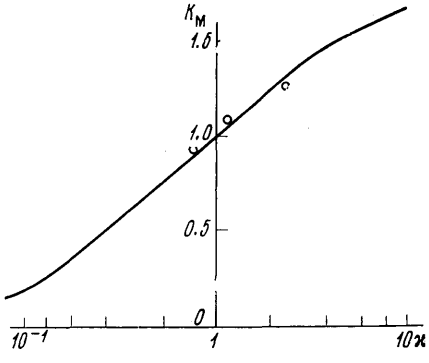


Figure 2. Theoretical variation of the microheterogeneity coefficient with the reactivity ratio of the functional groups of the intermonomer in stage-by-stage interbipolycondensation (see Table 6 for the significance of the experimental points).

The parameters of the distributions defined by Eqn. (8) are expressed in terms of the initial mole fraction σ_R and σ_S of the comonomers and their conversions p_A and p_B:

$$\nu_{RR} = \alpha_R p_A^2, \; \nu_{SS} = \alpha_S p_B^2 . \quad (9)$$

As stated above, only the statistical copolymer is formed in the case considered by Beste. Calculation of the distribution of blocks with respect to length in the chains of arbitrary copolymers based directly on kinetic process equations leads to Eqns. (8) precisely[47]. However, it is significant that the parameters of distributions (8) are not determined in the general case by relations (9) but are expressed in terms of the concentrations of the triads T_{RR} and T_{SS} and the initial concentrations of the comonomers:

$$\nu_{RR} = \frac{2T_{RR}}{[A]_0}, \; \nu_{SS} = \frac{2T_{SS}}{[B]_0} . \quad (10)$$

When the functional groups of the initial compounds are independent, Eqns. (10) become identical with Eqns. (9).

For long macrochains, the microheterogeneity coefficient may be related to the parameters of distributions (8):

$$K_M = 2 - \nu_{RR} - \nu_{SS} . \quad (11)$$

Since for a statistical copolymer $K_M = 1$, according to Eqn. (11) the relation $\nu_{RR} + \nu_{SS} = 1$ should hold. In the general case of chains of arbitrary length, K_M cannot be expressed in terms of the parameters ν_{RR} and ν_{SS}.

In order to describe the structure of the copolymers obtained as a result of interbipolycondensation, it is necessary to specify with the aid of functions (8) two parameters ν_{RR} and ν_{SS}. By virtue of the condition $\nu_{RR} + \nu_{SS} = 1$, it is sufficient to specify only one independent parameter for a statistical copolymer. Eqns. (1), (2), (8), (11), and (10) show that, in order they characterise quantitatively the microheterogeneity of polycondensation copolymers, it is sufficient to determine the proportions of triads of various types. Calculation of the triad concentrations directly on the basis of the kinetic process mechanism[6,47] makes it possible to relate the nature of the distribution of units in the chains to the process conditions and the reactivities of the monomers. On the other hand, the proportions of triads of various types in the copolymer can be determined experimentally with a high degree of accuracy by ^{1}H NMR.

Copolycondensation processes involving initial compounds of the ARC type capable of self-condensation have characteristics qualitatively different from those discussed above. It has been noted[6] that, in the bipolycondensation of monomers the functional groups of which are independent, a statistical copolymer is not formed. This last factor constitutes a significant difference between the above process and interbipolycondensation where the condition of the independence of the functional groups of the intermonomer was itself sufficient for the formation of products with a statistical distribution of units. Only a simplified case of comonomers of the A–R–C and B–S–C types, when both contain the same functional group C and all the groups are independent, has been considered in quantitative terms. For this special case, Lavalou[48] derived equations describing the composition and subsequently the microheterogeneity coefficient of the copolymer was calculated[6]:

$$K_M = \frac{2(\alpha_R p_B + \alpha_S p_A)(p_A + p_B)}{[p_A + \alpha_R (p_A + p_B)][p_B + \alpha_S (p_A + p_B)]} . \quad (12)$$

The value of K_M defined by Eqn. (8) is always greater than unity and tends to it with increase of the degree of reaction. Consequently, despite the fact that intermediates in the above bipolycondensation process exhibit a tendency towards an alternation of units, the distribution of the latter in the high-molecular-weight copolymer is statistical. When the reactivities of all four functional groups of the comonomers are different, statistical copolymers are not formed at all.

V. APPLICATION OF HIGH-RESOLUTION NMR SPECTROSCOPY IN THE ANALYSIS OF POLYCONDENSATION COPOLYMERS

NMR spectroscopy is at present the principal physical research technique whereby it is possible to characterise quantitatively the distribution of the units in the macromolecules of copolymers. The essential feature of this method, which allows the determination of the contents of homo- and hetero-triads in copolymers, is that the chemical shifts of the protons of the intermonomer residue depend in some cases on which comonomer residues adjoin the given compound in the polymer chain. Fig. 3 shows that the chemical shifts of the signals corresponding to the phenylene proton of the terephthalic acid residue in the NMR spectra of polyesters vary with its environment. The integrated signal intensities are proportional to the relative contents of triads in the copolymer.

Only a few studies in which high-resolution NMR was used to determine the structures of polycondensation copolymers have now been published and these refer exclusively to polyesters.

The first time when high-resolution NMR was used to investigate the structures of polycondensation copolymers was published in 1965 when Harada and Veda[49] investigated the compositions and structures of ethylene glycol,

diethylene glycol, and terephthalic acid copolyesters (Table 5, No. 4).

NMR spectroscopy was also used by Yamadero and Murano[50] and Slonim and coworkers[51] to determine the structures of a number of polyesters synthesised by equilibrium polycondensation in the melt (Table 5). Hamb[52] used this method to investigate the structures of polyesters synthesised by the reaction of poly(ethylene terephthalate) with terephthalic acid and the diacetate of di-2,2-(4-hydroxyphenyl)propane (Table 5, No. 3). In 1972 it proved possible to employ NMR for the elucidation of the structures of copolyesters based on ethylene glycol and terephthalic and isophthalic acids[53]. The introduction of chelate complexes of europium into the test solution enabled the author to increase the difference between the chemical shifts of the signals due to the ethylene glycol residues entering into different triads.

In 1972 Korshak et al.[54] published for the first time data on the structures of copolymers obtained by non-equilibrium polycondensation. They employed terephthalic acid chloride as the intermonomer and various bisphenols and hexamethylene glycol as the comonomers. This choice of initial compounds enabled the authors to determine quantitatively by NMR spectroscopy to within 5% the contents of homo- and hetero-triads in copolyesters (Table 5, No. 1).

Table 5 shows that copolyesters based on intermonomers such as ethylene glycol or terephthalic acid are suitable for the quantitative determination of triads by high-resolution NMR.

Despite certain limitations of the applicability of the NMR method in the study of polycondensation copolymers, its importance in such applications is very great. The method opens up wide prospects for the elucidation of the overall dependence of the compositions and structures of polycondensation copolymers on the reactivities of the initial compounds and reaction conditions.

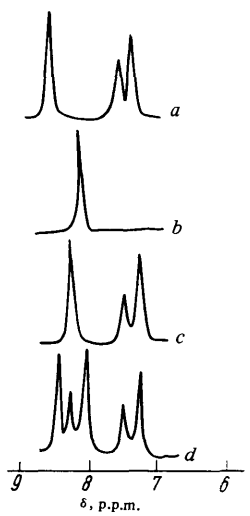


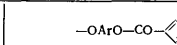
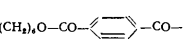
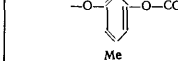
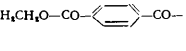
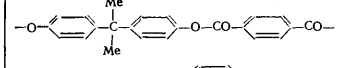
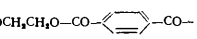
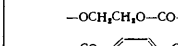
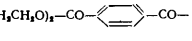
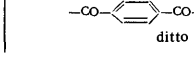
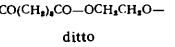
Figure 3. The NMR spectra of tetrachloroethane solutions of polyterephthalates (Table 5, No. 1): *a*) 2,2-bis-(3-chloro-4-hydroxyphenyl)propane (dichlorodian); *b*) hexamethylene glycol; *c*) regular alternation of dichlorodian and hexamethylene glycol residues; *d*) statistical distribution of dichlorodian and hexamethylene glycol residues.

VI. EXPERIMENTAL DATA FOR THE COMPOSITIONS AND STRUCTURES OF COPOLYMERS OBTAINED BY NON-EQUILIBRIUM COPOLYCONDENSATION IN HOMOGENEOUS SYSTEMS

The experimental data for the effect of various factors, including reaction time, for the compositions and structures of copolymers obtained by non-equilibrium copolycondensation in homogeneous systems were not available in 1972. However, it was postulated that under the conditions of non-equilibrium condensation it is difficult to obtain copolymers with a statistical distribution of fundamental units[7,8,30,35].

In her report at the Third Microsymposium on Polycondensation Processes, Turska[7] emphasised that "when there is a difference between the reactivities of the initial comonomers, there are altogether no grounds for the expectation of a statistical distribution of monomer residues" in copolycondensation products obtained under non-equilibrium conditions.

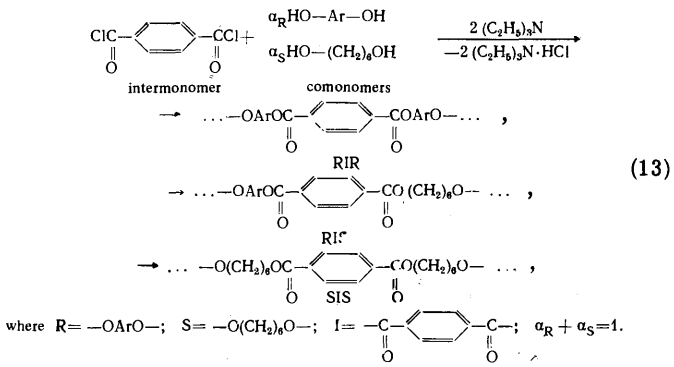
Table 5. Polycondensation copolymers investigated by high-resolution NMR spectroscopy.

No.	Fundamental unit of copolymer		Chemical shifts of group "I" protons in triads (δ scale), p.p.m.			Conditions of recording of NMR spectra*			References
	R—I	S—I	R—I—R	R—I—S	S—I—S	temp., °C	solvent for copolymers	concn. of soln.	
1			8.4	8.3	8.1	130	*sym*-Tetrachloroethane	16%	54
						34	ditto	10%	32
2			7.95	(7.85)**	7.77	70	Trifluoroacetic acid	0,05 g ml^{-1}	50
3			8.35	8.25	8.15	—	ditto	—	52
4			(8.06)**	(8.03)**	8.0	80	*o*-Chlorophenol	0.1 g ml^{-1}	49
5			4.47	4.27	4.07	70	Trifluoroacetic acid	0.05g ml^{-1}	50
6	ditto	ditto	4.70	4.47	4.27	125	*sym*-Tetrachloroethane	15—20%	51

*All the NMR spectra were recorded at a frequency of 60 MHz.

**Found from the NMR spectra quoted by the authors for the copolymers with a 1 : 1 molar ratio of the comonomer residues.

In 1972 Korshak and coworkers[29,54] were the first to report experimental data for the compositions and structures of copolymers obtained by non-equilibrium polycondensation in solution. They chose for investigation polyesters obtained by acceptor-catalytic copolycondensation in the presence of tertiary amines:



(13)

Acceptor-catalytic polyesterification is known to be a typical non-equilibrium process in which exchange reactions hardly occur[55].

The relative contents of the RIR, SIS, and RIS triads in the copolyesters obtained were determined by NMR spectroscopy (Table 6, No. 1 and Fig. 3). The degree of disorder in the copolymer (B) calculated in accordance with Yamadero and Murano's scheme[50] is identical in its significance to the microheterogeneity coefficient K_M.

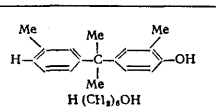
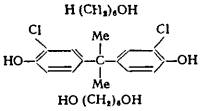
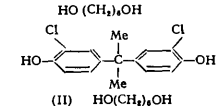
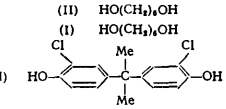
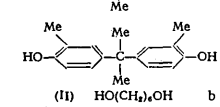
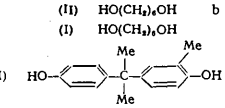
1. Single-stage Copolycondensation

The study of the dependence of the composition of the copolymers obtained by single-stage non-equilibrium polycondensation in homogeneous systems yielded results, which agreed fully with the earlier hypotheses (see, for example, Turska[7]). It was found that the composition of the linear copolymers formed by non-equilibrium copolycondensation in solution for low degrees of reaction with respect to the intermonomer is enriched in the more reactive comonomer[32]. Subsequently the fraction of the less reactive comonomer in the copolymer increases and, when the reaction reaches completion, the composition of the resulting high-molecular-weight compound is the same as that of the mixture of initial compounds. An example of such a process is provided by the acceptor-catalytic copolycondensation of terephthaloyl chloride with 2,2-bis-(3-chloro-4-hydroxyphenyl)propane and hexamethylene glycol in the presence of triethylamine (under these conditions, the reactivity of the bisphenol is more than 30 times greater than that of the glycol[27]). Fig. 4 shows that, as the reaction proceeds, the contents of the comonomers (bisphenol and glycol) in the copolyester become equal to their initial values, i.e. $P_R = P_S = 0.5$.

Turska[7] reported the results of the fractionation of two copolymers synthesised by single-stage non-equilibrium copolycondensation, which indicate the inhomogeneity of the compositions of the products.

Interesting experimental data were obtained in a study of the structures of the copolymers formed by non-equilibrium copolycondensation in solution using the single-

Table 6. The structures of the copolyesters obtained by non-equilibrium acceptor-catalytic polycondensation in solution in one (Nos. 1 and 2) and two (Nos. 3–6) stages[29,32].

No.	Initial diol formula		r	Content of triads, m.f.[c] R—I—R	R—I—S	S—I—S	Content of units, m.f.[c] P_R	P_S	Mean block length L_R	L_S	Microheterogeneity coefficient K_M
1		a	5.3	0.19	0.62	0.19	0.50	0.50	1.6	1.6	1.24
2		a	33	0.22	0.56	0.22	0.50	0.50	1.8	1.8	1.12
3		b	∞	0.25	0.54	0.21	0.53	0.47	1.9	1.8	1.09
4			∞	0.16	0.64	0.20	0.48	0.52	1.5	1.6	1.28
5		b	∞	0.19	0.64	0.17	0.51	0.49	1.6	1.5	1.28
6			∞	0.16	0.66	0.18	0.49	0.51	1.5	1.5	1.32

a. triethylamine (0.01 mole) added to dichloroethane solution (25 ml) of terephthaloyl chloride (0.005 mole), bisphenol (0.0025 mole), and hexamethylene glycol (0.0025 mole) at 40°C and polyesterification continued for 1 h.
b. Triethylamine (0.01 mole) added to dichloroethane solution (25 ml) of terephthaloyl chloride (0.005 mole) and bisphenol (0.0025 mole) at 40°C. Hexamethylene glycol (0.0025 mole) introduced after 30 min and the reaction continued for a further 1 h.
c. m.f. = mole fraction.

stage method[29,32]. Thus it was established that the structure of the macromolecules formed in single-stage non-equilibrium copolycondensation (see Scheme 13) in homogeneous systems depends little on the differences between the reactivities of the comonomers (Table 6, Nos. 1 and 2). Moreover, it was shown that the distribution of units in the polymer chains of the copolyesters obtained under the above conditions is close to the statistical distribution. The microheterogeneity coefficient is approximately unity and is independent of the molar ratio of the comonomers in the initial mixture.

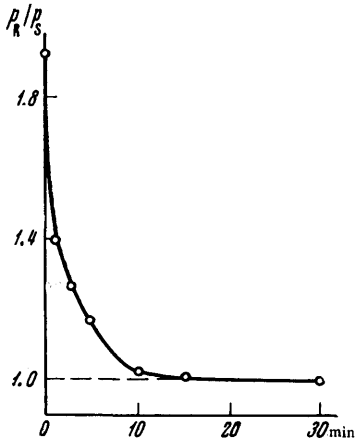


Figure 4. Variation of the composition of the copoly-terephthalate of 2,2-bis-(3-chloro-4-hydroxyphenyl)propane dichlorodian and hexamethylene glycol with reaction time (see footnotes in Table 6).

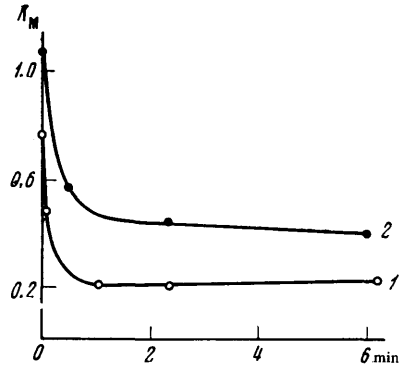


Figure 5. Variation of the microheterogeneity coefficient of the copolyester with the time taken to introduce the solution of terephthalic acid chloride into the solutions of the other components: 1) 2,2-bis-(3-chloro-4-hydroxyphenyl)propane dichlorodian, hexamethylene glycol, and triethylamine; 2) 2,2-bis-(3-methyl-4-hydroxyphenyl)propane dimethyldian, hexamethylene glycol, and triethylamine (dichloroethane, 30°C).

The study of the influence of the duration of the copolycondensation on the structure of the copolymers obtained by the reaction of terephthaloyl chloride with certain pairs of comonomers having different copolycondensation constants showed[32] that at the beginning of the reaction the copolymer is enriched in the RI units containing the more reactive comonomer, but subsequently the relative contents of the units formed by different comonomers become equalised (Table 7). It is important to emphasise that the coefficient of microheterogeneity of copolyesters remains constant throughout the reaction, the value of K_M showing that the distribution of fundamental units in the macromolecules is nearly statistical.

Table 7. Dependence of the composition and structure of the copolyesters of 2,2-bis-(3-chloro-4-hydroxyphenyl)propane, hexamethylene glycol and terephthalic acid on the duration of copolyesterification*.

Reaction time, min	Yield of copolyester, %	η_{int} (0.5% soln. in *sym*-tetrachloroethane at 25°C), dl g^{-1}	Content of fundamental units, m.f.**		Microheterogeneity coefficient K_M
			P_R	P_S	
0.5	59	0.08	0.66	0.34	1.09
1	60	0.09	0.58	0.42	1.19
3	76	0.11	0.56	0.44	1.10
5	81	0.14	0.54	0.46	1.17
10	89	0.19	0.51	0.49	1.12
15	91	0.25	0.51	0.49	1.12
60	93	0.52	0.50	0.50	1.12

*See footnote a to Table 6.
**m.f. = mole fraction.

Thus, as a result of the difference (r = 5.3–33) between the reactivities of the comonomers, the composition of the copolymer changes as non-equilibrium polycondensation proceeds, while the distribution of fundamental units remains constant and nearly statistical.

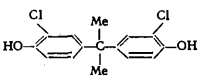
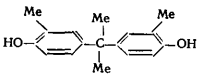
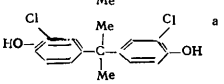
2. Two-stage Copolycondensation

One of the methods of synthesising block-copolymers proposed previously by a number of workers involves the introduction of the comonomers into the reaction sphere stage by stage[8,30]. However, until recently there were no experimental data confirming the block structure of the copolymers prepared by this procedure.

It is interesting to note that the stage-by-stage method of introduction of the initial comonomers into the reaction zone as it were simulates the case of simultaneous copolycondensation when the copolycondensation constant for the comonomers is high ($r \to \infty$). Initially fragments comprising the intermonomer and the more reactive comonomer are formed and the less reactive comonomer only then begins to react with these fragments, which leads to the formation of the copolymer.

The first study of the copolyester obtained by two-stage non-equilibrium copolycondensation in solution was published in 1972.[29] Certain results of these investigations are presented in Table 6 (Nos. 3–6). It was found that the distribution of units in the chains of the copolyesters obtained by stage-by-stage polycondensation is nearly statistical. Thus, even the simulation of an infinite difference between the reactivities of the comonomers did not lead to the formation of block-copolymers. When the stage-by-stage polycondensation of terephthaloyl dichloride with 2,2-bis-(3-chloro-4-hydroxyphenyl)propane and hexamethylene glycol was carried out for different molar ratios of the latter, block-copolymers were not obtained either.

Table 8. The structures of the copolyesters obtained by two-stage non-equilibrium acceptor-catalytic polyesterification in the presence of triethylamine with gradual introduction of the intermonomer in stage I (dichloroethane, 40°C)[29,32,56].

No.	Order of addition of initial compounds		Content of units, m.f.[c]		Block length		Microheterogeneity coefficient K_M
	stage I	stage II	P_R	P_S	L_R	L_S	
1	$HO(CH_2)_6OH$[a]		0.48	0.52	1.6	1.7	1.23
2	ditto [b]	ditto [a]	0.47	0.53	5.6	6.0	0.34
3		$HO(CH_2)_6OH$	0.54	0.46	3.6	3.0	0.61
4	 [a]	ditto	0.53	0.47	9.1	7.7	0.24
5	ditto [b]	»	0.58	0.42	12.5	10.0	0.18

a. In the first stage terephthaloyl chloride was added in the solid state over a period of 1 s.
b. Terephthaloyl chloride added in dichloroethane solution over a period of 15 min.
c. m.f. = mole fraction.

3. Gradual Introduction of the Intermonomer into the Reaction Zone

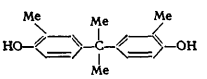
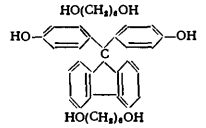
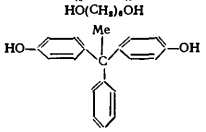
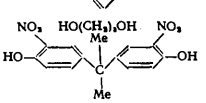
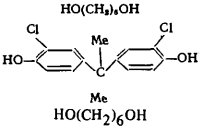
Block-copolyesters were synthesised with a gradual introduction of the intermonomer (terephthaloyl chloride) into the reaction zone[29,32,56], both in the solid state and as a solution. In the first case the rate of introduction of the intermonomer into the reaction zone was determined by the rate of its dissolution and in the second case by the rate of injection.

In the stage-by-stage synthesis of comonomers in the presence of triethylamine when terephthaloyl chloride was introduced in the first stage in the solid state, a statistical or a block sequence of fundamental units in the macromolecules was obtained depending on the reactivity of the diol (Table 8, Nos. 1, 3, and 4). The use of the relatively unreactive hexamethylene glycol in the first stage leads to a statistical distribution of the fundamental units in the copolyester. An increase of the reactivity of the comonomer used in the first stage causes a decrease of the microheterogeneity coefficient of the copolyester and a corresponding increase in block length. Thus the smallest microheterogeneity coefficient of the copolymers was obtained when dichlorodian ($r \simeq 33$), i.e. the most reactive of the comonomers investigated, was employed in the first stage.

The addition of solid terephthaloyl chloride to a solution of diols with $r \neq 1$ in the presence of triethylamine also leads to the formation of block-copolymers (Table 9). It was established that the size of the blocks in the copolyesters[54] depends significantly on the particular difference between the reactivities of the comonomers or, what amounts to the same thing, on their copolycondensation constant. An increase of the copolycondensation constant promotes an increase in block size and a decrease in the coefficient of microheterogeneity of the copolymers (Table 9).

The formation of block-copolymers with $K_M = 0.2-0.4$ when the intermonomer is introduced in the solid state into a solution of the comonomers with $r \gg 1$ was noted for different molar ratios of the initial diols[32]. However, the formation of block-copolymers on introduction of solid terephthalic acid did not occur when the acceptor-catalyst employed was pyridine[32], which is much less effective than

Table 9. The structures of the copolyesters obtained by single-stage non-equilibrium acceptor-catalytic polyesterification in the presence of triethylamine with the introduction of solid terephthaloyl chloride into the reaction zone (dichloroethane, 40°C).[54]

No.	Initial diols (1 : 1 molar ratio)		Content of units, m.f.*		Block length		Microheterogeneity coefficient K_M
	formula	r	P_R	P_S	L_R	L_S	
1		5.3	0.50	0.50	4.4	4.4	0.46
2		12.6	0.50	0.50	5.6	5.6	0.36
3		13.3	0.51	0.49	5.4	5.1	0.38
4		31	0.49	0.51	8.2	8.5	0.24
5		33	0.50	0.50	9.2	9.2	0.22

*m.f. = mole fraction.

triethylamine. Indeed, it has been shown for the benzoylation of *p*-nitrophenol in dioxan at 30°C that the reaction rate constant decreases from 6.48×10^{-2} to 5.92×10^{-2} litre^2 mole^{-2} s^{-1} on passing from triethylamine to pyridine[57]. Since acylation in the presence of pyridine is much slower, there is sufficient time for the complete dissolution of the solid intermonomer introduced into the reaction space, which leads to its greater involvement in the reaction and hence to the conditions of single-stage non-equilibrium copolycondensation in solution. Consequently, regardless

of the difference between the reactivities of the comonomers, in the presence of pyridine copolymers with a statistical distribution of units were obtained under these conditions[32]. In the presence of pyridine block-copolymers were obtained only after a slow introduction of the intermonomer solution into a solution of the comonomers and the acceptor-catalyst. This method of introduction of the intermonomer was investigated in detail in relation to the reaction of terephthaloyl chloride with two pairs of comonomers in the presence of triethylamine in dichloroethane solution at 40°C (Table 8, Nos. 2 and 5 and Fig. 5)[29,32,56]. It was observed that, when the entire solution of terephthalic acid chloride is added at once to the solution of the bisphenol, hexamethylene glycol, and triethylamine, the microheterogeneity coefficient of the resulting copolymers approaches the value corresponding to a statistical distribution of units. When the intermonomer is introduced into the reaction zone over a fairly long period, the microheterogeneity coefficient of the copolyester decreases, tending to a limiting value, which depends on the copolycondensation constant of the comonomers (Fig. 5).

4. Three-stage Copolycondensation

As already mentioned above, in three-stage copolycondensation each comonomer undergoes polycondensation with the intermonomer in different reaction zones. In one case the intermonomer is introduced in excess relative to the comonomer and in the other in a deficient amount such that the overall molar amounts of the functional groups of the intermonomer and the comonomers are the same in both reaction spaces. At the end of the polycondensation in the two systems, the latter are combined, and the reaction begins to proceed between the intermediates formed in the first stages.

Table 10. The structures of the copolyesters obtained by three-stage non-equilibrium acceptor-catalytic polycondensation in the presence of triethylamine (dichloroethane, 40°C).

No.	Molar ratios		Content of units, m.f.*		Block length		Microheterogeneity coefficient K_M
	terephthaloyl chloride: dichlorodian	terephthaloyl chloride: hexamethylene glycol	P_R	P_S	L_R	L_S	
1	0.5:1	1.5:1	0.48	0.52	2.4	2.6	0.81
2	0.7:1	1.3:1	0.45	0.55	3.2	3.8	0.57
3	0.9:1	1.1:1	0.44	0.56	5.9	7.7	0.30

*m.f. = mole fraction.

Many workers[30,31] use three-stage copolycondensation as a method of synthesising block-copolymers, although until recently there was no experimental evidence for the structures of the resulting copolymers. One could only presume that the block length in such copolymers depends on the molecular weight of the products obtained in the first stages. Thus, it was reasonable to conclude that, with increase or decrease of the excess of the intermonomer, relative to the comonomers, the block length in the copolymers will change.

It was established quite recently that the degree of disorder and length of the blocks in the copolymer are determined to a considerable extent by the deviation from equivalent amounts of the functional groups (Table 10).[32] Thus the smallest microheterogeneity coefficient of the copolymer was obtained for the closest approach to the equivalent amounts of the groups of the intermonomer and comonomer at each of the first stages (Table 10, No. 3).

Thus, experimental study of the structures of the copolymers obtained by non-equilibrium copolycondensation in a homogeneous system yielded the following relations. 1. The introduction of the entire intermonomer into the reaction zone at the beginning of non-equilibrium copolycondensation leads to the formation of copolymers with a nearly statistical distribution of polymer chain units regardless of the differences between the reactivities of the comonomers employed. 2. The stage-by-stage introduction of the comonomers into the reaction zone is not a sufficient condition for the formation of block-copolymers. 3. For the synthesis of copolymers with a block structure by single-stage non-equilibrium polycondensation in solution, it is necessary that the reactivities of the initial comonomers should be different and that the rate of introduction of the intermonomer is lower than the rate of its reaction with the more reactive monomer. By varying the above factors, it is possible to obtain block-copolymers with different lengths of the block fragments.

VII. COMPARISON OF THEORY WITH EXPERIMENT

The above experimental data are not only in qualitative agreement with the theory of homogeneous non-equilibrium copolycondensation developed by Kuchanov[6,47] but also provide a quantitative confirmation of the calculated relations. The microheterogeneity coefficients of copolyesters determined by ^{1}H NMR can be conveniently compared with the theoretical K_M, which are determined, in particular, by the relative reactivities of the functional groups of the initial compounds. Since the comonomers employed in the investigations[29,32,54,56] contained independent functional groups, and those in the intermonomer were interdependent, the interbipolycondensation processes involving them are generally characterised by four kinetic chain propagation constants. The microheterogeneity coefficients of the copolymers obtained in such processes are determined by three independent parameters κ_A, κ_B, and r_1. The first two of these are equal to the ratio of the reactivities of the first and second groups of the intermonomer in its reactions with each of the comonomers and the parameter r_1 characterises the relative reactivities of the comonomers in their reactions with the first groups of the intercomponent. The reactivities of the comonomers in relation to the second groups of the intercomponents (parameter r_2) can be simply expressed in terms of the above parameters: $r_2 = 2_1\kappa_A/\kappa_B$. When the condition $\kappa_A = \kappa_B = \kappa_1$ holds, it is evident that $r_1 = r_2 = r$ and therefore K_M is determined by the two parameters x and r. When $\kappa_A \neq \kappa_B$, the concept of the relative reactivity parameter of the comonomers r becomes purely qualitative, since only r_1 and r_2 have a definite quantitative significance.

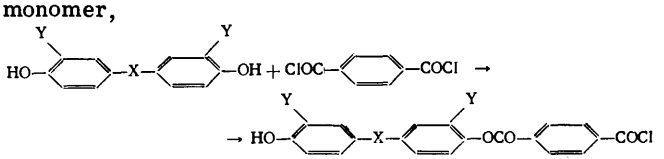
It is simplest to compare theory with experiment in two-stage interbipolycondensation where the second comonomer is introduced into the reaction zone after the first has already reacted. For a specified ratio of the comonomers, K_M is determined according to theory only by the value of κ for the comonomer introduced first and is independent of the parameters r_1 and r_2. The theoretical curve relating K_M to κ for different amounts of the

comonomers is presented in Fig. 2. The Figure also compares the experimental K_M taken from Table 6 taking into account the κ from Table 1. Clearly there is a good quantitative agreement between the theoretical and experimental data, the difference between them being within the limits of experimental error. It follows from Fig. 2, that the parameters κ found, on the one hand, by analysing the structures of the copolymers and, on the other, from kinetic measurements virtually agree. In the first case the synthesis of copolyesters is carried out in dichloroethane solution and in the second the acylation rate constants are determined in dioxan. The small differences between the values of κ obtained by the two independent methods permit the conclusion that the solvent has only a weak influence on the ratio of the rate constants for the first and second groups of the intermonomer. One must emphasise that the solvent does have a very marked influence on the absolute values of the acylation rate constants. For example, the rate constant for the reaction of *p*-nitrophenol with benzoyl chloride in the presence of triethylamine increases almost by four powers of ten on passing from dioxan to dichloroethane [28].

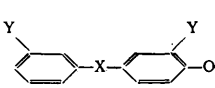
Fig. 1 illustrates the influence of the relative reactivity parameter of the comonomers r on the structure of the copolymers obtained on slow introduction of the intermonomer. It shows that all the experimental points taken from Table 9, with the exception of one, fit satisfactorily on the theoretical $K_M - r$ curve defined by Eqns. (6)–(7) for $\alpha_R = \alpha_S = 0.5$. This agreement should be regarded as satisfactory bearing in mind that, both in the derivation of Eqns. (6) and (7) and in the experimental determination of r in accordance with Eqn. (5), no account was taken of the difference between κ_A and κ_B. The latter factor implies that the values of r quoted in Table 4 yield in general only a preliminary estimate of the relative reactivities of the comonomers. Since r is intermediate between r_1 and $r_2 = r_1\kappa_A/\kappa_B$, the estimate will be more accurate the smaller the difference between κ_A and κ_B and hence between r_1 and r_2. It is therefore clear that the r quoted in Table 4 for 2,2-bis-(3-methyl-4-hydroxyphenyl)propane and 2,2-bis-(3-chloro-4-hydroxyphenyl)propane, which differ appreciably in the values of the parameter κ, constitute only a conventional quantitative characteristic of the relative reactivities of the above comonomers. This explains why the experimental K_M for 2,2-bis-(3-methyl-4-hydroxyphenyl)propane does not fit on the theoretical curve in Fig. 1.

Comparison of r for the bisphenol–glycol comonomer pair and the values of κ for terephthaloyl chloride (in relation to the phenolic component) found by any procedure shows a definite relation between these parameters. By comparing the results presented in Tables 1 and 4, it is seen that κ diminishes with increase of r. The reactivity of the bisphenol increases, i.e. r increases, in the case of non-equilibrium polycondensation under consideration when substituents Y with more pronounced electron-accepting properties are introduced into its molecule [15].

When a bisphenol of this kind interacts with the intermonomer,



a new group



the electron-accepting properties of which are to a large extent determined by the nature of Y, is formed in place of the COCl group. As the electron-accepting properties of Y become more marked, the reactivity of the second acid chloride group of the intermonomer may become not only comparable to that of the first group but may actually exceed it, which is in fact observed in the reaction of many substituted phenols with terephthaloyl chloride. The experimental microheterogeneity coefficients of the products obtained when all the initial compounds are introduced at once, are presented in Table 6. It is noteworthy that these values are close to the K_M for the copolymers formed in two-stage interbipolycondensation (Table 6). This result, which also follows from theory, is quite reasonable for comonomer pairs with a large value of the parameter r. As a result of the appreciable difference between reactivities, mainly the more reactive comonomer (bisphenol) reacts at the beginning of the process and hexamethylene glycol reacts only after some time when the bisphenol has been exhausted. Thus the distribution of units in the copolymer is close to that obtained in the two-stage process, when the bisphenol is added first. Since the above rule holds better the greater the difference between the reactivities of the comonomers, the maximum departure from it is to be expected for the bisphenol with the smallest value of r in relation to hexamethylene glycol. This conclusion is confirmed by the experimental data in Table 6.

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Thus, the results presented in the review show that a quantitative theory of non-equilibrium copolycondensation in homogeneous systems has now been established. The conclusions of this theory have been quite convincingly confirmed by experimental results. Further study on copolycondensation should probably have the following two aims. Firstly, a similar theoretical and experimental treatment of non-equilibrium copolycondensation processes in heterophase systems is needed. Secondly, systematic studies are required on the influence of the compositions and structures of the polycondensation copolymers on their properties. The solution of this problem will make it possible to employ successfully the data quoted in this review for the synthesis of copolymers with specified properties.

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Institute of Organic Derivatives of the Elements, USSR Academy of Sciences, Moscow

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System of Retention Indices and Its Physicochemical Application

R.V.Golovnya and Yu.N.Arsen'ev

The system of retention indices widely used in gas chromatography is reviewed. Methods of calculating indices are examined, their accuracy and reproducibility, and the effect on the index of parameters of the gas-chromatographic experiment (temperature, pressure, velocity of carrier gas, and quantity of stationary phase in the column). Systems resembling retention indices are described, problems of polarity, selectivity, and effectiveness of separation are discussed, and the physicochemical application of indices to calculate various thermodynamic functions is considered. A list of 252 references is included.

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I. INTRODUCTION

Choice of the best mode of expressing retention data has hitherto been one of the highly debated problems of gas chromatography[1-5].

The use of retention parameters in the form of absolute units, e.g. as the specific volume retained, is not generally accepted, since change in the sorbent during prolonged use, inadequate accuracy in measuring the speed of the carrier gas and the pressure at the inlet to the column, and also unsatisfactory reproducibility of the column temperature lead to uncompensated errors[2-4]. Furthermore, this determination is very laborious[6]. Relative retention volumes, which are less dependent on the conditions of analysis, can be determined more simply and with sufficient accuracy[1,7,8]. However, this method requires a multiplicity of standards, which in fact makes correlation between different publications impossible[2,3].

These difficulties in determining universal gas-chromatographic characteristics led Kováts[9,10] to introduce retention indices. In the opinion of many investigators this system is the most systematic and convenient for generalising retention data. Several reviews have been published[2,3,11-14], and a large number of original papers, mainly concerned with the use of retention indices for identification purposes. The aim of the present Review is to give a comprehensive survey of indices as retention parameters and to reveal the main fields of and prospects for application of this system in physicochemical calculations. This permits an approach both to certain analytical problems (identification of substances, choice of selective stationary phases, selection of conditions of separation) and to several physicochemical problems (study of structure, determination of physicochemical properties from chromatographic data, and investigation of interactions in solution).

II. METHODS OF CALCULATION OF RETENTION INDICES

The elution maxima of individual members of the homologous series of n-alkanes form the fixed points of the system of indices. In the original definition of retention indices[9] Kováts proposed to use only n-alkanes with an even number of carbon atoms. He assumed that an appreciable difference in chromatographic behaviour would be observed in the successive identification of all the members of a homologous series. However, this limitation was subsequently removed[15], and the retention index came to be determined by means of the equation

$$I = 100\frac{\lg V_X - \lg V_n}{\lg V_{n+1} - \lg V_n} + 100n \qquad (1)$$

provided that $V_n \leqslant V_X \leqslant V_{n+1}$, where V_X, V_n, and V_{n+1} are the corrected retention volumes of the test substance and of the standard n-alkanes containing n and $n + 1$ carbon atoms respectively. It follows from Eqn. (1) that any absolute or relative (reduced to the same standard) retention parameters[2,3,8,15], corrected for the dead space, or the corresponding distances on the chromatogram, can be used as initial parameters for calculating retention indices.

The linear dependence of the logarithm of the retention volume of an n-alkane on the number n of carbon atoms[2,3,16-18]

$$\lg V_n = a + bn \qquad (2)$$

where b depends solely on temperature and on the properties of the stationary phase[19-21], will yield the simpler equation

$$I = 100\frac{\lg V_X - \lg V_n}{b} + 100n \qquad (3)$$

for calculating retention indices[2]. Calculation of retention indices by means of Eqn. (3) is based on a "theoretical" series constructed from 3 or 4 experimental retention times for normal hydrocarbons having $n \geqslant 6$.

In work with capillary columns the gas-dynamic pulse at the start of an experiment produces an appreciable scatter in the values of I calculated by means of Eqn. (3).[22] It was suggested that the reproducibility could be improved by calculating initially the relative retention $V_{X,\,st}$ and then converting it into the retention index by means of the equation

$$I = 100\frac{\lg (V_{X,\,st} \cdot V_{st,\,n})}{b} + 100n\,. \qquad (4)$$

Preliminary determinations had been made of b and of the relative retention of the standard with respect to n-alkanes $V_{st,n}$.

Graphical methods [23-25], nomograms [26-28], and a special slide-rule [15] have been suggested to simplify calculations of retention indices. Computer programmes have also been written for calculating indices [29-31].

Not only n-alkanes but any other components whose indices under the given conditions are known (I_1 and I_2) can be used to determine the retention indices of unknown components. The Kováts formula then becomes [25]

$$I_X = (I_2 - I_1)\frac{\lg V_X - \lg V_1}{\lg V_2 - \lg V_1} + I_1 . \quad (5)$$

Equation (5) is advantageous for prolonged analyses, e.g. when a capillary column is used, since it is unnecessary to reuse the standard n-alkanes. Furthermore, formula (5) may find application for calculating retention indices on polar stationary phases if Eqn. (2) does not apply.

Theoretical Calculation

Cases quite often arise in analytical practice when it is necessary to calculate retention indices theoretically. Linear equations are very often used for this purpose, relating retention indices with the number of carbon atoms in the molecule or with the boiling point, or else the calculation is based on the difference in retention indices on columns differing in polarity [32-54]. Such an approach underlies the standard-free identification of substances. In several cases relations of this type give only a first approximation to the index, owing to departures from linearity.

Retention indices can be determined additively from structural increments [11,14,32-40,44,47,55-68]. According to Tatevskii's theory [69] additivity calculations are based on the general relation [70]

$$\lg L = \sum_{i,j}^{k} n_{i,j}\Gamma_{i,j} \quad (6)$$

where L is the elution characteristic, $\Gamma_{i,j}$ the contribution of the structural unit, and $n_{i,j}$ the number of structural units in the molecule. Temperature coefficients of retention indices are sometimes used in calculating the latter from structural increments [71-74]. The validity and practical application of additivity calculations have been shown by many workers [10,32-42,45,75-84], but there is no doubt about their approximate character.

Retention indices for solutions that are nearly ideal can be calculated from the vapour pressures of the components at the temperature of the column [85]:

$$I_{p^0} = 100\frac{\lg p^0_X - \lg p^0_n}{\lg p^0_{n+1} - \lg p^0_n} + 100n \quad (7)$$

where p^0_X, p^0_n, and p^0_{n+1} are the vapour pressures of the test substance X and the standard hydrocarbons containing n and $n+1$ carbon atoms respectively. Tourres [86] showed that in non-polar systems I_{p^0} and the experimental I have almost the same temperature dependence, since the variation of the activity coefficients with temperature can be neglected in this case [87]. With the vapour pressure at various temperatures (and hence I_{p^0}) known, therefore, it is possible to predict both the behaviour of substances and their degree of separation. The so called standard retention index I_{st} [88], calculated from the boiling points by means of the formula

$$I_{st} = 100\frac{\lg T_{bp(X)} - \lg T_{bp(n)}}{\lg T_{bp(n+1)} - \lg T_{bp(n)}} + 100n \quad (8)$$

must be regarded as a particular case of I_{p^0}.

A more exact equation for calculating retention indices of hydrocarbons on non-polar stationary phases, proposed by Dimov and Shopov [89,90], involved the molar volumes:

$$I_{p^0,v^0} = 100\frac{\ln\left(\frac{p^0_X v^0_X}{p^0_n v^0_n}\right) - \left(\frac{v^0_X - v^0_n}{v^0_1}\right)}{\ln\left(\frac{p^0_{n+1} v^0_{n+1}}{p^0_n v^0_n}\right) - \left(\frac{v^0_{n+1} - v^0_n}{v^0_1}\right)} + 100n \quad (9)$$

where v^0_X, v^0_n, v^0_{n+1}, and v^0_1 are the molar volumes of the substance X, the normal hydrocarbons containing n and $n+1$ carbon atoms, and the stationary phase respectively. A thermodynamic proof of Eqn. (9) has been given by Hammers and de Ligny [91]. However, the "physicochemical indices" obtained in this way differ to some extent from the experimental values I. Conversion from I_{p^0,v^0} to I requires the introduction of corrections equal to the mean difference between I and I_{p^0,v^0} for hydrocarbons of the same class [92].

Unfortunately, theoretical calculation of retention indices by means of Eqns. (7)-(9) is possibly only for hydrocarbons and non-polar stationary phases, which considerably diminishes the significance of these relations.

Thus the foundation of the gas-chromatographic study of real systems remains as before the experimental determination of the retention index by means of Eqns. (1) and (3).

III. PARAMETERS RESEMBLING RETENTION INDICES

The indices I_{p^0}, I_{st}, and $I_{p^0v^0}$ discussed in Section II (Eqns. 7-9) are completely analogous to the Kováts index. Retentions are replaced by physicochemical constants.

The Kováts indices were followed by several similar scales, but these found limited application in gas chromatography. Examples are the "methylene unit" [93-95], which is identical with the retention index divided by 100, the "effective molecular weight" [79,96-98], where the molecular weights of n-alkanes are used as fixed points on the scale, and the "carbon numbers" [99,100] ("equivalent chain length" [101]), which are convenient for the analysis of aliphatic acids and their methyl esters. All these systems, being particular cases of the general Kováts system, possess closely similar properties. The mathematical equivalence of the above systems was shown by Guerin and Banks [102].

In several cases, e.g. in high-temperature gas-chromatographic analyses or with the use of strongly polar phases, n-alkanes are not always convenient as standard substances [103]. Swoboda [104], without changing the general construction of the Kováts system, proposed that the standards should be chemically similar to the test compounds. Thus "steroid numbers" [93-95] proved convenient in the gas-chromatographic analysis of steroids, the "phenyl number" [105] in the chromatography of linear polyphenyls, and the "siloxane index" [106-108] for the identification of organosilicon derivatives. An analogous system was proposed for the characterisation of high-boiling (up to 500 °C and above) fused aromatic and heteroaromatic compounds, where comparisons are based on polyacene hydrocarbons—benzene, naphthalene, anthracene, tetracene, etc. [109]

A rational generalisation of these systems is the dimensionless parameter φ[110]. Standard compounds belonging to the same homologous series as the test substance are used in calculating φ:

$$\frac{\lg V_{g\,X} - \lg V_{g1}}{\lg V_{g2} - \lg V_{g1}} = \varphi = \frac{T_{bp(X)} - T_{bp(1)}}{T_{bp(2)} - T_{bp(1)}} \qquad (10)$$

where V_gX, V_{g1}, V_{g2}, $T_{bp(X)}$, $T_{bp(1)}$, and $T_{bp(2)}$ are the retention volumes and the boiling points of the related compounds (X unknown, and *1* and *2* known). The parameter φ was shown to be constant, independent of the temperature of the analysis and the composition of the stationary phase. However, it cannot be recommended for the identification of complicated mixtures, comprising substances belonging to different homologous series, owing to ambiguity in the choice of standards and the absence of a natural "zero point". Retention indices have an undoubted advantage in this respect.

In order to avoid comparatively laborious stages in determining the "dead space" and taking logarithms in calculating Kováts indices, it was suggested that an "arithmetic index"[111-113] should be calculated by means of the equation

$$I_A = 100\,\frac{t_X - t_n}{t_{n+1} - t_n} + 100n \qquad (11)$$

where t_X, t_n, and t_{n+1} are uncorrected retention times for the test substance X and the standard n-alkanes. Equation (11) is sometimes written without the coefficients 100.[111,112,114] The arithmetic index has been used to estimate partition and activity coefficients[114]. However, the usefulness of the arithmetic index as a retention parameter is debatable[113,115,116], since no thermodynamic interpretation has yet been found. The theoretical possibility of the graphical conversion of I_A into I has been established[114]. An equation has recently been deduced[117] linking the arithmetic index with the retention index:

$$\frac{I - 100n}{100} = \frac{\lg\left[1 + \frac{I_A - 100n}{100}(D-1)\right]}{\lg D} \qquad (12)$$

where

$$D = \frac{t_{n+1} - t_n}{t_n - t_{n-1}}$$

t_{n-1}, t_n, and t_{n+1} being uncorrected retention times of successive n-alkanes. Furthermore, D = antilog b, where b is the coefficient in Eqn. (2). A thermodynamic basis for I_A may, perhaps, be found by the application of Eqn. (12).

IV. ACCURACY AND REPRODUCIBILITY OF RETENTION INDICES

For a long time the accuracy and the reproducibility of retention indices remained an open question. In connection with the increasing importance of gas chromatography in qualitative analysis and physicochemical research, interest has arisen during recent years in the precise measurement of retention parameters[23,118-124]. These aspects of retention indices calculated by means of Eqn. (1) can be extended equally to the simpler equation (3), since the two equations give values of comparable accuracy[17].

Tests of the reproducibility of indices determined on standard instruments in different laboratories[125] gave a standard deviation of ±1 on squalane and dinonyl phthalate and ±3 on [polyethylene glycol] PEG-400; the divergence in the indices on a polar stationary phase depends on the size of the sample of n-alkanes introduced into the chromatograph. It was shown later[126] that reproducible retention indices can be obtained even on such a polar phase as oxy-$\beta\beta'$-dipropionitrile if the samples of n-alkanes used in solution are 0.002–0.007 μl, when the linear portion of the partition isotherm is reached.

Loewenguth[127] gave a similar statistical assessment of the reproducibility of retention indices. Reproducibility is influenced mainly by the accuracy with which retention times and column temperatures are measured. The latter factor is especially significant in the analysis of compounds with a large temperature coefficient of the index dI/dT. Kaiser[23] reaches the same conclusion.

The first precision measurements of retention indices were made on ordinary and deuteriated squalane, with a maximum discrepancy of 0.06.[16,128] Schomburg et al.[129] used an on-line computer to measure retention indices with a reproducibility of ±0.03–0.05. Cramers et al.[130] achieved the same reproducibility (±0.03) without using an electronic computer. Analysis of these results showed that, in order to obtain reproducible retention indices, careful attention should be paid to measuring and stabilising the temperature of the thermostat; an inert material of uniform grain size should be used as solid support; the length and diameter of the column, the effectiveness of separation of the mixture, the rate of flow of the carrier gas, and the inlet and outlet pressures to and from the column must be taken into account; and the retention times of test substances and standard n-alkanes must be measured accurately[119].

Whereas the reproducibility of retention indices can be judged from how well the calculated values of I converge in a series of experiments, it is a more complicated task to determine the accuracy of the calculation of indices. A rigorous approach to this problem based on the principles of mathematical statistics was first made by Takács and Králik[131,132]. A solution of the problem was obtained independently by Uhdeova[118], but only in general form.

Analysis of the extended error formula deduced by Takács and Králik (called the Erdey equation) showed that the accuracy with which retention indices are determined depends on the absolute retention times of the test substance t_X, the n-alkanes t_n and t_{n+1}, and the unsorbed gas t_M, as well as the arithmetic mean errors of their determination. With a favourable choice of chromatographic conditions, when t_n, t_X, $t_{n+1} \gg t_M$, errors in the determination of the "dead space" can be neglected. From this the important conclusion can be drawn that, in the determination of retention indices, direct measurement of t_M can be replaced by indirect calculation, e.g. by use of the equation of Peterson and Hirsch[133]. For squalane the determination of t_M with respect to methane and hydrogen and by the Peterson–Hirsch method[133] was shown by Cramers et al.[130] to give identical results, with a reproducibility of the index of ±0.03.

Thus indices can be obtained with a minimum error. It is also noteworthy that the precision measurement of other retention parameters has not been studied so thoroughly, and this constitutes an indubitable advantage of the Kováts system of indices.

V. TEMPERATURE DEPENDENCE OF RETENTION INDICES AND ITS USE IN GAS CHROMATOGRAPHY WITH TEMPERATURE PROGRAMMING

In the early gas-chromatographic investigations Kováts and Wehrli [9,10] established a linear correlation between the index and the temperature of the analysis. They proposed that three parameters—(*a*) the index at the given temperature, (*b*) the temperature coefficient $10dI/dT$ for a 10 deg change in temperature, and (*c*) the temperature limits within which the indices were measured—should be stated to express the temperature dependence of retention indices. The temperature dependence was subsequently studied by many investigators [3,15,71,76,78,85,87,134-141]. The relation was found to be hyperbolic over a wide temperature range [78,134].

Allowing for the temperature dependence of the corrected retention volume [142], Takács et al. [12,142-144] showed by rigorous mathematics that the temperature dependence of retention indices obeys a hyperbolic equation with three constants, resembling Antoine's equation

$$I_{(T)} = A + \frac{B}{T + C} \qquad (13)$$

where A, B, and C depend on the properties of the test substance and the stationary phase. Experimental verification of Eqn. (13) is accomplished by means of an electronic computer [145,146]. The hyperbola (13) is usually essentially linear in the gas-chromatographic temperature range [143]. Fig. 1 shows the general form of the temperature dependence of the retention index of propan-1-ol on PEG-400.

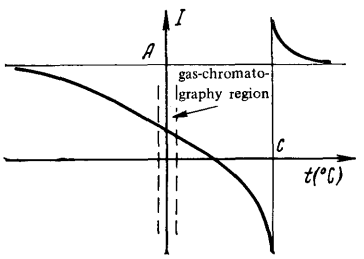


Figure 1. General form of temperature dependence of retention index of propan-1-ol for the phase PEG-400. [143]

The temperature coefficient dI/dT is an important characteristic of the substance and the stationary phase, and can be used for identification purposes [72,140,147]. In several investigations [73,87] the coefficient $dI/d(1/T)$ has been used to establish structure. The differential dI/dT was employed [148,149] to calculate the equivalent isothermal index in the case of linear temperature programming. If at least one component in a solute–stationary phase system is polar, the sign of the differential will depend on the properties of the system for the individual case [91,150-153].

Study of the temperature dependence of the retention indices of various hydrocarbons [71,86,87,91,154] showed that the coefficient is affected by the number and the steric arrangement of the side-chains in the molecule. Hammers and de Ligny [91] gave a rigorous thermodynamic basis to the coefficient dI/dT, and established that its magnitude is determined by the free energy and the entropy of vaporisation of the substance undergoing analysis.

The temperature dependence of retention indices has been examined thermodynamically for ideal solutions [155]. The general dependence of the index on the temperature and the enthalpies and entropies of vaporisation was shown for three simple hypotheses—(i) that the enthalpy of evaporation of n-alkanes is constant, (ii) that the enthalpy decreases linearly with rise in temperature, and (iii) that the enthalpy varies in conformity with the Thiesen (Watson) equation [156]—among which the third assumption gives the best agreement between calculated and experimental indices.

The Kováts index has proved a convenient retention parameter not only in isothermal but also in temperature-programmed gas chromatography. An equation has been proposed for calculations [105,135,136,157-159], based on a nearly linear dependence of the elution temperature of n-alkanes on the number of carbon atoms:

$$I_{tpr} = 100\frac{T_{r_X} - T_{r_n}}{T_{r_{n+1}} - T_{r_n}} + 100n \qquad (14)$$

where I_{tpr} is the retention index of the test substance with temperature programming, and T_{rX}, T_{rn}, and $T_{r,n+1}$ are the retention temperatures of the test substance and of n-alkanes containing n and $n + 1$ carbon atoms respectively. A theoretical deduction of Eqn. (14) has recently been achieved by Takemura [160] on the basis of his previously established [161,162] linear relation between the isothermal relative retention and the relative retention with temperature programming.

The index calculated by means of formula (14) usually differs from, but is quite close to, the isothermal index at some equivalent temperature T_{eq}. Thus Guiochon [135,136] found that programmed indices agree best with the isothermal value at 20 deg below the retention temperature. Habgood and Harris showed [157] that, with cyclic hydrocarbons, the indices with temperature programming correspond to the isothermal values at a temperature 30–50 deg below T_r. Giddings [163] proposed the correlation equation $T_{eq} = 0.92T_r$.

The opinion has become established among specialists in this field that, with temperature programming, the retention index varies little with quite a wide choice of analysis conditions—initial temperature, rate of programming, and speed of carrier gas [135,136,157,158,163].

The experimental conditions have an appreciable effect on the index with programming, especially when substances showing a large temperature coefficient are analysed on polar phases [148,149]. An equation was deduced to allow for the experimental parameters—rate of linear programming β, temperature coefficient of index dI/dT, and retention temperature of substance T_r:

$$I_{T_0/\beta} = I_{T_0} + \frac{\beta T_r}{2} \cdot \frac{dI}{dT} . \qquad (15)$$

Comparison of the calculated equivalent isothermal indices I_{T_r-20}, $I_{0.92T_r}$ and $I_{T_0/\beta}$ showed that $I_{T_0/\beta}$ will give the best agreement with the experimental value I_{tpr} [148,149]. This is because $I_{T_0/\beta}$ takes into account not only T_r but also the conditions of the programmed experiment (T_0, β, t). The equivalent isothermal index $I_{T_0/\beta}$ has been used with linear temperature programming for the qualitative analysis of monocarbonyl compounds in the volatile components of certain foodstuffs [164,165]. Robinson and Odell [88] extended

the mathematical approach[148,149] to non-linear temperature programming (with the temperature raised in steps), and suggested that the mean temperature of the elution and the temperature coefficient of the index should be taken into account in calculating retention indices.

Erdey et al.[12,166,167] integrated Eqn. (13) from the initial temperature T_0 to the retention temperature T_r, and obtained a general equation for the equivalent isothermal index in temperature-programmed gas chromatography:

$$I_{eq} = A + \frac{2.3B \cdot \lg\left(\frac{T_r + C}{T_0 + C}\right)}{T_r - T_0} \qquad (16)$$

where A, B, and C are the constants in Eqn. (13) determined from the isothermal indices measured at three different temperatures[143]. If these constants are known, I_{eq} can be calculated by means of (16) without the need to chromatograph n-alkanes. Because the computation of A, B, and C is laborious, the determination of I_{eq} by means of Eqn. (16) is extremely complicated.

Formulae (15) and (16) are essentially similar, although the former was deduced on the hypothesis of a linear temperature dependence of retention indices, and the latter from a hyperbolic dependence. Because the hyperbola usually has a linear section in the gas-chromatographic temperature range[143], Eqns. (15) and (16) should give the same calculated result. Erdey et al.[167] found that equivalent isothermal indices calculated by means of the two equations for benzene and PEG-1500 as stationary phase differed at most by ±1. From a practical point of view, therefore, use of the simpler equation (15) is to be preferred, despite its less general character.

Thus the temperature dependence of retention indices obeys in general a hyperbolic law, although the hyperbola usually has a linear section in the gas-chromatographic temperature range. This enables retention indices at different temperatures to be handled very simply, and validates the use of the temperature coefficient dI/dT. It also presents greater opportunities for the widespread use of Eqn. (15) in gas chromatography with linear programming of temperature.

VI. EFFECT OF THE INDEX OF PARAMETERS OF GAS-CHROMATOGRAPHIC EXPERIMENT

The principles of classical equilibrium chromatography, when the temperature of analysis T, the speed of the carrier gas w, the input pressure to the column p_i, and the pressure drop factor j_2^3 are constant, are generally used in calculating retention indices, as with other retention parameters[131]. Under these conditions the fall in pressure in the column and the speed of the carrier gas in numerator and denominator of Eqns. (1) and (3) cancel out, with small variations in T, w, and p_i partly or completely balanced out. This forms the basis for the conclusion that the system of indices is stable with respect to experimental conditions[2,3,15,168]. Nevertheless, it is useful to examine the effect of various experimental variables on the retention index.

1. Retention Index and Speed of Carrier Gas

Guerin and Banks[102] found that the constant b in Eqn. (3) is unaffected by changing the speed of the carrier gas from 40 to 200 ml min^{-1}.

Equation (1) was transformed[169,170] to contain rates of flow of the carrier gas w (instead of specific retention volumes) and the constants in the equation for the dependence of retention time on w. Changing the speed of the carrier gas from 1 to 500 ml min^{-1} left the indices almost unchanged. This enables retention indices to be used to identify components in gas chromatography with programming of the gas flow.

2. Retention Index and Pressure in System

Two main factors—considerable non-ideality of the gas phase and solubility of the carrier gas in the stationary phase—complicate the interpretation of retention indices and the calculation of thermodynamic functions from chromatographic data obtained at high pressures[54]. Vigdergauz and Semkin[171-173] demonstrated the effect of non-ideality of the gas at high pressures on the retention indices of hydrocarbons. They showed that changing from helium to carbon dioxide and raising the pressure in the column to 15 atm are accompanied by changes in the retention indices, and in some cases even the sequence in which substances are eluted may change. Retention indices at high pressures have been used for the calculation of second virial coefficients[54,171-173].

Unfortunately, the effect of increased pressure on retention characteristics, including Kováts indices, has still been comparatively little studied.

3. Retention Index and Quantity of Stationary Phase in Column

The relative retention volumes of polar substances (in relation to non-polar substances) are strongly dependent on the proportions of highly polar stationary phases when these are below 5%.[174] This makes it difficult to identify components of a mixture by means either of relative retention volumes or of retention indices. Kováts[15] recommended working at high proportions of the stationary phase in order to obtain good reproducibility of the retention indices. However, this diminishes the efficiency of the column, the height of a theoretical plate is considerably more strongly dependent on the speed of the carrier gas, and the duration of the analysis increases[175]. In order to achieve maximum separating power with a chromatographic column, therefore, the optimum quantity of stationary phase must be taken. With diatomites this varies within 5–10% of the total weight of sorbent[176].

In the analysis of unsaturated and substituted methyl esters of C_{16}–C_{18} acids on the non-polar stationary phases Apiezon L and SE-30 the retention indices are almost independent of the quantity of the stationary phase on the solid support, whereas a very considerable variation is found on the polar polyethylene glycol succinate[177]. The chromatography of polar substances shows that the nature of the adsorbent has an appreciable effect on the index. Thus the retention indices of alcohols on squalane columns become smaller when Chromosorb V is replaced by Chromosorb G[179].

Bonastre et al.[178] obtained an equation for calculating retention indices that took into account adsorption phenomena in the column:

$$I = 100\,\frac{\lg\dfrac{\left|V_g^\infty + \frac{h}{\Pi} + \hbar\left(\frac{1}{\Pi} - \frac{1}{10}\right)\right|_x}{\left|V_g^\infty + \frac{h}{\Pi} + \hbar\left(\frac{1}{\Pi} - \frac{1}{10}\right)\right|_n}}{\lg\dfrac{\left|V_g^\infty + \frac{h}{\Pi} + \hbar\left(\frac{1}{\Pi} - \frac{1}{10}\right)\right|_{n+1}}{\left|V_g^\infty + \frac{h}{\Pi} + \hbar\left(\frac{1}{\Pi} - \frac{1}{10}\right)\right|_n}} + 100n \qquad (17)$$

where V_g^∞ is the specific retention volume with maximum possible percentage impregnation Π, and the coefficient h and $\hbar$ represent adsorption on the film of stationary phase and on the solid support respectively. With the standard n-alkanes $\hbar \simeq 0$. With PEG-20 000 and thio-ββ-dipropionitrile as the stationary phases, polytetrafluoroethylene and Chromosorb P as solid supports, and a large number of substances belonging to various classes these workers showed that the retention indices increase with increase in the degree of impregnation Π, in conformity with Eqn. (17), and approach their limiting values I^∞. It was found also that the constant $\hbar$ can be substantially diminished by the use of inert supports. A generalised equation for the retention volume in gas-liquid chromatography which in addition to solution in the stationary phase takes into account adsorption at its interfaces with the carrier gas and adsorbent has also been proposed [180,181].

On the whole it can be accepted that retention indices are extremely stable over a wide range of rates of flow of the carrier gas at column pressures that are usual in analytical gas chromatography. However, the quantity of stationary phase in the column (especially one of high polarity) has an appreciable effect on the index. In order to obtain reproducible indices, therefore, inert solid supports must be used, the same quantity of stationary phase (not less than 5–10 wt.%), and with highly polar phases minimum samples of the standard n-alkanes in order to reach the linear portion of the partition isotherm.

VII. CHARACTERISATION OF STATIONARY PHASES AND COLUMNS BASED ON RETENTION INDICES (POLARITY, DONOR AND ACCEPTOR POWER, SELECTIVITY, EFFECTIVENESS OF SEPARATION)

Problems of forecasting the chromatographic value of stationary phases and columns from the theory of dissolution and the physicochemical properties of solute and solvent have been solved during recent years [4,176,182,183]. In order to make a preliminary estimate of retention parameters, many attempts were undertaken to relate them to the thermodynamic, electrical, and geometric properties of stationary phases. Many groups of substances exhibit a certain dependence of the relative retention parameters on the electrical characteristics (dipole moment, dielectric constant, polarisability, refraction) of the stationary phase or of the separable components) [184–189].

Polarity

The terms "polar", "weakly polar", "non-polar", etc. are too inexact to characterise stationary phases. As Kováts showed [15], the concept of "polarity" is convenient, and in some cases sufficient, to describe many effects, but it cannot be expressed by a single parameter.

The polarity of stationary phases determined from retention characteristics is ultimately a function of the cohesion potential: i.e. it depends on the contribution by orientation, induction, and dispersion forces. Together with these, donor–acceptor interactions are especially important in gas chromatography [190]. The energy of van der Waals interaction, except for the dispersion component, depends on the temperature, so that polarity is also a function of temperature [188,191].

Rohrschneider [192] originally proposed a graphical method, in which the stationary phases were arranged along the horizontal axis with the polarities 0 and 100 assigned to squalane and oxy-ββ′-dipropionitrile respectively, which enabled stationary phases to be characterised by appropriate polarity indices. Almost the same approach to classifying phases was being followed by several other workers [191,193–205], except that the standard substances used were not butadiene and butane, but methanol and butane, acetylene and ethane, benzene and hexane, two n-alkanes, etc. Sakharov has shown [185,206] that all these methods derive from the general relation

$$\lg V = B_1 \lg V_{st} + B_2 \qquad (18)$$

where V and V_{st} are the retention volumes of the substance and the standard respectively, B_1 is a constant representing the polarity of the substance undergoing analysis, B_2 is another constant, and $\lg V_{st}$ measures the polarity of the stationary phase. However, the considerable uncertainty in the choice of standard substances imposes considerable limitations on this method.

The system of retention indices provides a more convenient form for expressing differences in the character of stationary phases. This assignment is based on the difference between the interaction of the substance with the test phase and with a phase which is by definition regarded as non-polar (squalane, Apiezon).

Wehrli and Kováts [10,15] suggested measuring the difference ΔI between the retention indices for compounds of general formula RX, where R is a hydrocarbon radical containing six or more carbon atoms, and X a functional group. Since $\Delta I = 0$ when X = H, the proposed scale begins at zero. It is termed the "dispersion of retention" of the stationary phase.

Developing this idea, Rohrschneider [207–210] suggested that the polarity of the column depends not only on the nature of the stationary phase but also on the type of substance analysed. The polarity of a stationary phase must therefore be assessed simultaneously with respect to a whole group of compounds possessing diverse donor–acceptor properties. This is a more rigorous approach to solving the problem. Rohrschneider originally proposed one- and three-term equations, but these did not find wide application. Later he worked out a general five-term polarity system, which has been recommended for the widest use in gas chromatography [211–213]. The general equation is

$$\Delta I = ax + by + cz + du + es \qquad (19)$$

where a, b, c, d, and e are polarity factors of the stationary phase, and x, y, z, u, and s are polarity factors of the substances undergoing analysis. Having determined the polarity factors of 22 stationary phases with respect to the compounds adopted as standards (benzene, ethanol, butan-2-one, nitromethane, and pyridine) and those of 30 substances, Rohrschneider calculated 660 indices with errors not exceeding 4–6. Accurate measurements have shown that the values of the Rohrschneider constants depend on the size of sample introduced [214], so that this size must be indicated when such constants are published.

Without changing Rohrschneider's general concept, McReynolds [215] suggested a different list of standards—including benzene, butanol, pentan-2-one, nitropropane, pyridine, and five other substances for solving particular problems—which are more convenient experimentally. McReynolds compiled a table of differences in retention indices of ten test substances for various stationary phases. The list of stationary phases comprises approximately 200 items.

Takács et al. [212,213] has recently shown, by rearranging Eqn. (19), that the interaction between test substances and

stationary phases can be characterised not only by the difference between but also by the ratio of the indices. They obtained the equation

$$I_X^P = I_X^S \sum_{i=1}^{5} f_i s_i \qquad (20)$$

where I_X is the isothermal retention index of the substance X, the letters P and S represent a polar stationary phase and squalane respectively, $f_i = I^P/I^S$ is the ith polar factor, i is the serial number of Rohrschneider's or McReynolds' standard substance, and

$$\frac{a}{100}\cdot\frac{I_1^S}{I_X^S} = s_1;\ \frac{b}{100}\cdot\frac{I_2^S}{I_X^S} = s_2;\ \cdots\ \frac{e}{100}\cdot\frac{I_5^S}{I_X^S} = s_5$$

are specific factors for the substance, characterising the molecular structure and the interaction potential. Equation (20) represents more accurately the effect of the specific factors s_i for substances and gives better agreement between calculated and experimental values of the index than does Eqn. (19).

Another proposed method for determining the polarity of a stationary phase is based on the equation [85,178,216]

$$P = (k^0 - k)\cdot 10^5 = 10^3 \lg(\gamma_{n+1}^{\infty}/\gamma_n^{\infty}) \qquad (21)$$

in which γ_n^{∞} and γ_{n+1}^{∞} are the activity coefficients of the n-alkanes containing n and $n+1$ carbon atoms. The quantities k^0 and k are related to the retention indices I_1 and I_2 of two substances by indices $I_{p_{(1)}^0}$ and $I_{p_{(2)}^0}$, computed from the vapour pressures (Eqn. 7) and by the relative activity coefficient $\gamma_{1,2}^{\infty}$:

$$\lg\gamma_{1,2}^{\infty} = k^0(I_{p_{(1)}^0} - I_{p_{(2)}^0}) - k(I_1 - I_2). \qquad (22)$$

Bonastre et al. [178] then suggested that, to allow for adsorption phenomena on the surface of the adsorbent and the stationary phase, indices should be calculated by means of Eqn. (17) and k replaced by k^{∞}, corresponding to the largest proportion of stationary phase. In this case the polarity computed by means of formula (21) will then be determined almost entirely by the dissolution of the substance in the stationary phase, which is more accurate.

Comparison of the Chovin–Lebbe [193-195,201,202] and the Bonastre–Grenier [85,178,216] methods for determining the polarity of stationary phases shows that physically the former consists in measuring the constant b (Eqn. 2), which is equal to the increment of the partial molar free energy of sorption per methylene group $\Delta G_{s,CH_2}$ in an n-alkane [19]. Thus in this method the polarity is estimated solely from the dispersion component of the total interaction potential, and increase in polarity correlates with a decrease in b. In contrast Bonastre and Grenier assess polarity not on the basis of the above increment but on $\Delta G^E_{CH_2}$, which measures the departure of the system from Raoult's law. The more the ratio $\gamma_{n+1}^{\infty}/\gamma_n^{\infty}$ in Eqn. (21) differs from unity, and hence $\Delta G^E_{CH_2}$ from zero, the more polar is the stationary phase. Strictly speaking, however, Eqn. (21) defines not the polarity but the selectivity of the stationary phase with respect to the n-alkanes, since, apart from a constant (2.3 RT), the logarithm of the relative activity coefficient is the "empirical" selectivity—the difference between the partial molar excess (free) energies of sorption [17,183].

Kováts and Weisz [217] also used retention indices to examine the polarity of stationary phases. If the total free energy of dissolution is determined by the work of separation (the energy of a hole), by a dispersion term, by a polar term, and by the energy of donor–acceptor interaction, the sum of the last two terms is proportional to the difference between the retention indices of the test substance on the column with a given solvent and a standard non-polar phase.

Thus a survey of published information shows that Rohrschneider's method, with the standard compounds proposed by McReynolds, is the most widely used at the present time for assessing the polarity of stationary phases.

Donor and Acceptor Power

Using Brown's triangular method [218], Guiochon et al. [61,219] showed that retention indices could be employed to assess such important properties of a phase as its donor and acceptor power. The method involves constructing a triangular diagram, on which are plotted the normalised retention indices of an electron acceptor (1,4-dioxan), an electron donor (1,1,2-trichloroethane), and a neutral compound (n-decane). Use of a triangular diagram provides a simple and graphic procedure for assessing the donor and acceptor power of a stationary phase, but the method has no significant advantages over Rohrschneider's system.

Selectivity

The selectivity of a stationary phase in gas–liquid chromatography is a static characteristic independent of kinetic factors, e.g. plate height [220]. It is measured [4,182,183,220] by the relative activity coefficient or by the difference in the free energies of mixing $\Delta\Delta G^E_{i,j}$. In this connection retention indices provide the most rational system, since they represent the relative retention with n-alkanes as a scale of standards of the same type. Several equations have been suggested [17,20,21,221] for estimating the selectivity of a stationary phase from retention indices:

$$\lg\alpha_{i,j} = \frac{b\,\delta I_{i,j}}{100} = -\lg(\gamma_{i,j}^{\infty} p_{i,j}^0) \qquad (23)$$

$$\Delta\Delta G_{i,j}^E = -2.3RT\left(\frac{b\,\delta I_{i,j}}{100} + \lg p_{i,j}^0\right) \qquad (24)$$

$$\Delta\Delta H_{i,j}^E = -2.3RT\left[\frac{\delta I_{i,j}}{100}\cdot\frac{\partial b}{\partial 1/T} + \frac{b}{100}\cdot\frac{\partial(\delta I_{i,j})}{\partial 1/T} + \cdot\frac{1}{2.3p_{i,j}^0}\frac{\partial p_{i,j}^0}{\partial 1/T}\right] \qquad (25)$$

$$\Delta\Delta S_{i,j}^E = \frac{\Delta\Delta H_{i,j}^E - \Delta\Delta G_{i,j}^E}{T} \qquad (26)$$

where $\alpha_{i,j}$ is the separation factor, $\Delta\Delta G^E_{i,j}$, $\Delta\Delta H^E_{i,j}$, and $\Delta\Delta S^E_{i,j}$ are the differences between the free energies, enthalpies, and entropies of mixing, b is a constant in Eqn. (2), $\delta I_{i,j} = I_i - I_j$ is the difference between the retention indices of two substances, $p^0_{i,j}$ is the relative vapour pressure with the column at temperature T°K, and i and j are the compounds under examination.

Equations (23)–(26) have enabled a successful choice to be made of selective columns for the analysis of carbonyl [222] and sulphur-containing compounds [17,20,21,221,223]. In the latter case eleven stationary phases were examined, for which values of $\Delta\Delta G^E_{i,j}$ were calculated by means of Eqn. (24) using n-hexanethiol, dipropyl sulphide, and diethyl disulphide as examples (results in Table). The maximum values of this difference were obtained for columns containing oxy-$\beta\beta'$-dipropionitrile, polyethylene glycols (PEG), and Triton X-305. It was found that oxy-$\beta\beta'$-dipropionitrile, previously regarded as the most

selective column for all sulphur-containing compounds[224], was not selective in the separation of thiols and sulphides (as $\Delta\Delta G^{E}_{2,1} \simeq \Delta\Delta G^{E}_{3,1}$—see Table), but was convenient in the separation of thiols and disulphides, and also of sulphides and disulphides.

Values $\Delta\Delta H^{E}_{i,j}$ and $\Delta\Delta S^{E}_{i,j}$ have been calculated by means of Eqns. (25) and (26) in order to reveal the nature of the selectivity of phases. It is found, for example, that the enthalpy factor predominates in the separation of dipropyl sulphide from diethyl disulphide on PEG-1000, but the entropy factor with hexanethiol and diethyl disulphide[17, 20, 21, 221].

Differences in partial molar free energies of mixing, calculated by means of Eqn. (24), of certain organosulphur compounds on various stationary phases[17, 40].

Stationary phase (at 60°C)	$\Delta\Delta G^{E}_{2,1}$	$\Delta\Delta G^{E}_{3,1}$	Stationary phase (at 60°C)	$\Delta\Delta G^{E}_{2,1}$	$\Delta\Delta G^{E}_{3,1}$	Stationary phase (at 130°C)	$\Delta\Delta G^{E}_{2,1}$	$\Delta\Delta G^{E}_{3,1}$
SE-30	—60	—100	Tritolyl phosphate	140	220	Apiezon M	10	20
Apiezon M	—70	—100	Triton X-305	200	330	Silicone DS-550	70	60
Silicone DS-200	—70	—120	PEG-1000	250	390	Triton X-305	220	290
Dinonyl phthalate + 5% diphenylamine	5	60	Oxy-ββ′-dipropionitrile	390	380	PEG-20000	260	370
Dinonyl phthalate	10	60						

Note. $\Delta\Delta G^{E}_{2,1}$ = difference between free energies of mixing of hexanethiol and diethyl disulphide.
$\Delta\Delta G^{E}_{3,1}$ = difference between free energies of mixing of dipropyl sulphide and diethyl disulphide.
Values of $\Delta\Delta G^{E}_{i,j}$ given in cal mole^{-1}.

Thus it has been shown experimentally that Eqns. (23)–(26) are extremely convenient for estimating the selectivity of stationary phases.

Effectiveness of Separation

The practical value of a chromatographic column is always determined by the fundamental possibility of separation and the time required for this separation. The effectiveness of separation is usually understood to refer to the blurring of the peak during the analysis[225].

Kováts[9] deduced the relation

$$\delta I \simeq 5\delta T_{bp} \qquad (27)$$

for the difference between the indices of two substances, from which can be estimated the minimum difference in boiling points necessary for the separation of isomers on non-polar stationary phases. However, Eqn. (27) is apparently not general in character, for it has recently been shown[51] with branched C_9 and C_{10} alkenes that the proportionality constant may differ considerably from 5, and assume values from 1.8 to 13.9.

A suggested criterion of separation R was determined by the ratio of the distance between the peak maxima to the sum of their half-widths at the base[226].

Instead of R Strickler and Kováts[19] used the $N\sigma$ criterion —the distance between the two separable substances expressed in σ-units (where σ is the half-width at the level of the point of inflection): separation does not occur if the distance between the peaks is equal to or less than 2σ. The 4σ criterion corresponds to adequate separation, and the 6σ criterion to almost complete separation. These workers compared the $N\sigma$ criterion with the difference between the retention indices of the separable substances δI, with the free energy of evaporation of the substances from the stationary phase per methylene group $\Delta G_{e(CH_2)} = b$—see Eqn. 2), and with the number of theoretical plates N_t:

$$\delta I = \frac{N\sigma\Phi}{\sqrt{N_t}}\left(1 + \frac{1}{k_i}\right) \qquad (28)$$

where k_i is the reduced retention time relative to the dead time, and

$$\Phi = \frac{100RT}{\Delta G_{e\,(CH_2)}}.$$

Struppe[227] proposed the use of a quantity Z which allowed for the progressive broadening of the peak on the chromatogram. In general, however, the calculation of this parameter is extremely complicated. From an analysis of values of Z this author concluded that, when highly efficient capillary columns are used, identification is possible only from the retention indices.

Ettre and Billeb[228] deduced an equation linking the difference in retention indices with the number of effective plates N_{eff} and the separation criterion R:

$$\delta I = \text{const} \cdot \lg \frac{\sqrt{N_{eff}}}{\sqrt{N_{eff}} - 4R} \qquad (29)$$

where the constant is $100/\lg(t_{R(n+1)}/t_{R(n)})$.

Rohrschneider showed[229] that R can be calculated from the difference between the retention indices by means of the equation

$$R = \frac{\delta I}{1.6998_I} \qquad (30)$$

where θ_I is the width of the peak at mid-height (in index units). He used an equation relating the logarithm of the relative retention to the difference in molar free energies of sorption to assign a rigorous thermodynamic meaning to the criterion R. He demonstrated also[230] that the effectiveness of separation depends on the polarity of the stationary phase expressed as in Eqn. (19).

In conclusion we note that the separation criterion R is used in gas chromatography far more often than are $N\sigma$ and Z, because R is most simply related to data obtained directly from a chromatogram. In order to estimate effectiveness of separation from retention indices, therefore, Eqn. (30) must evidently be used.

VIII. APPLICATION OF RETENTION INDICES IN THE CALCULATION OF PHYSICOCHEMICAL PARAMETERS

Tourres[86], as well as Bonastre and Grenier[85, 216], established the relation

$$I = 100\frac{\lg p^0_n - \lg p^0_X + \lg(\gamma^{\infty}_n/\gamma^{\infty}_X)}{\lg p^0_n - \lg p^0_{n+1} + \lg(\gamma^{\infty}_n/\gamma^{\infty}_{n+1})} + 100n \qquad (31)$$

between the relative activity coefficient, the vapour pressure, and the retention index, and used it to predict retention indices and to assess the polarity of stationary phases.

Vigdergauz and Semkin have recently suggested[54, 171–173] that retention indices at two elevated pressures P_1 and P_2 should be used to determine the mixed second virial coefficient B_{12}:

$$\frac{\Delta I}{\Delta P} = \frac{(I_1 - 100n)(\beta_{n+1} - \beta_n) - 100(\beta_X - \beta_n)}{-b_2} \qquad (32)$$

where $\Delta P = P_2 - P_1$, $\Delta I = I_2 - I_1$ measured at pressures

P_2 and P_1 in the column, $\beta_i = (2B_{12i} - v_i^\infty)/2.303RT$ ($i = x$, n, $n+1$), v_i^∞ is the molar volume of the liquid sorbate, and $b_2 = \lg(V_{g(n+1)_2}/V_{g(n)_2})$ is the logarithm of the relative retention volume of adjacent n-alkanes at pressure P_2. Calculation of B_{12} by means of Eqn. (32) is assumed to give more accurate results than its determination from the retention volumes.

Martynov and Vigdergauz [54] suggested a method for determining the density of alkanes at 20°C from the retention indices on squalane.

The most obvious though approximate method for determining the properties of substances is based on the relation, widely used in practical analysis, between the index or the logarithm of the relative retention and the boiling point, the number of carbon atoms in the molecule, or the logarithm of the vapour pressure [32-54, 59, 231-238].

Martin showed [239] that the free energy of sorption can be estimated by summing the structural increments for the molecule. Additivity of the retention index follows as a particular case [10, 56, 182, 240, 241]. The possibility thus appears of determining chromatographically the properties of compounds differing e.g. in quantity of substituents, number of multiple bonds, skeletal structure, etc.

Thermodynamic Nature of Index

Kováts [9] made the first attempt to find a thermodynamic basis for the retention index. Using the relation between the relative retention and the difference between the molar free energies of evaporation of the test substance and of the standard n-alkane $\Delta G_{e,X}$ and $\Delta G_{e,n}$, he established that

$$I = 100\frac{\Delta G_{e_X} - \Delta G_{e_n}}{\Delta G_{e\,(CH_2)}} + 100n\,. \qquad (33)$$

Comparison with Eqn. (3) shows that the constant b has a quite definite thermodynamic significance: it is the increment of the free energy of evaporation (dissolution) per methylene group [9, 17, 19, 91, 155, 242]. Kováts [9] obtained values of approximately 500 and 460 cal mole^{-1} for $\Delta G_{e(CH_2)}$ for Apiezon L and the Emulphor O respectively. He pointed out that, in the thermodynamic interpretation of retention indices, the free energies not only result from dissolution but also contain a contribution due to adsorption on the solid support and on the surface of the stationary phase.

Kováts and Weisz [217] showed later that the index measures the retention of a component on the scale of the standard chemical potentials of the n-alkanes:

$$I = 100\frac{\Delta\mu_X - \Delta\mu_n}{\Delta\mu_{n+1} - \Delta\mu_n} + 100n \qquad (34)$$

where $\Delta\mu_X$, $\Delta\mu_n$, and $\Delta\mu_{n+1}$ are the differences, between an ideal dilute solution and the ideal gas state, in the standard chemical potentials of the compound and of the n-alkanes. Formula (34) is most often written in terms of the Gibbs function [17, 20, 21, 91, 155, 242] or the free energy [54, 243].

Bach et al. [244] have recently used relations connecting the logarithm of the relative retention time with the thermodynamic functions of dissolution, Trouton's rule† and Klages' equation; these establish that the square of the boiling point is an additive function for homologues, to give an original thermodynamic proof of the system of retention indices.

†According to this rule the molar heat of evaporation of a non-associated liquid at its boiling point and atmospheric pressure is directly proportional to the absolute boiling point.

Thermodynamic Functions of Sorption

For a long time retention indices, because of their quite complicated thermodynamic interpretation (Eqn. 34), were not used in calculating the thermodynamic functions of the fundamental process in gas–liquid chromatography. It was found experimentally that the index varies linearly with the change in the molar free energy of sorption, and can serve as a measure of the latter when different substances are being compared [242].

The first systematic investigation of the thermodynamic application of retention indices [17, 20, 21, 221, 245, 246] led to deduction of the equations

$$\lg K_X = \frac{(I-100n)\lg\left(\frac{t_{R_{n+1}}}{t_{R_n}}\right)}{100} + \lg\frac{V_{g_n}^0 T\rho}{273}\,, \qquad (35)$$

$$\Delta G_{s_X} = -2.3RT\lg K_X\,, \qquad (36)$$

$$\Delta\Delta G_{s_X,\,n} = -0.023RT(I-100n)\lg\frac{t_{R_{n+1}}}{t_{R_n}}\,, \qquad (37)$$

$$\Delta H_{s_X} = \Delta H_{s_n} - 0.023R\left[\lg\left(\frac{t_{R_{n+1}}}{t_{R_n}}\right)\cdot\frac{\partial I}{\partial 1/T} + (I-100n)\frac{\partial}{\partial 1/T}\lg\left(\frac{t_{R_{n+1}}}{t_{R_n}}\right)\right], \qquad (38)$$

$$\frac{(I-100n)}{100}\lg\left(\frac{t_{R_{n+1}}}{t_{R_n}}\right) = \frac{-\Delta H_{s_X} + \Delta H_{s_n}}{2.3RT} + \frac{\Delta S_{s_X} - \Delta S_{s_n}}{2.3R}\,, \qquad (39)$$

enabling determinations to be made of partition coefficients K and partial molar enthalpies ΔH_s, entropies ΔS_s, and free energies ΔG_s of sorption (it is advisable to calculate excess thermodynamic functions and estimate the selectivity of chromatographic columns by means of Eqns. 23–26). In the above equations t_{R_n} and $t_{R_{n+1}}$ are the corrected retention times of the n-alkanes, and ρ is the density of the stationary phase. If $n \geqslant 6$, we can replace $\lg(t_{R_{n+1}}/t_{R_n})$ by the constant b of Eqn. (2). [17, 18] An equation analogous to (38) has since been published by other workers [91, 247, 248].

Since the dependence of $(I - 100n)b/100$ on $1/T$ (°K^{-1}) conforms closely to a linear law (Fig. 2), the calculation of enthalpies and entropies of sorption, as well as of separation factors, is considerably simplified by the graphical interpretation of Eqn. (39). [17, 20, 221]

The proposed method of calculating thermodynamic functions is simple and makes rather smaller demands on the experimental apparatus than does the classical method, based on the measurement of specific retention volumes. Thus it becomes unnecessary to measure the quantity of "active" phase in the column, the space velocity of the carrier gas, and the drop in pressure. Provided that $\Delta H_{s,n}$ and $\Delta S_{s,n}$ are known, neither the density nor the molecular mass of the stationary phase need be known in order to calculate $\Delta H_{s,X}$ and $\Delta S_{s,X}$ by means of Eqns. (38) and (39). With stationary phases that form athermal solutions with alkanes (hydrocarbons, phthalic esters, etc.), moreover, the tabulated value of the latent heat of evaporation can be used [243] instead of the standard function $\Delta H_{s,n}$.

With substances having retention indices exceeding 600, as mentioned above, $\lg(t_{R_{n+1}}/t_{R_n})$ can be replaced by the constant b in Eqn. (2), which expresses the linear dependence of the logarithm of the corrected retention volume of n-alkanes on the number of carbon atoms in the molecule. However, the legitimacy of using a linear equation has

hitherto been a controversial matter in gas–liquid chromatography. Several workers proposed non-linear equations to describe the gas-chromatographic behaviour of straight-chain hydrocarbons[203, 249, 250]. The accuracy of known equations has been assessed statistically by the use of regression analysis[17,18]. Experimental data on the retention of n-alkanes have been taken from McReynolds' tables[152] for thirteen stationary phases of varying polarity. The calculations were made on an electronic computer. The best of the non-linear equations, suggested by Sakharov and Voskov[250], has an accuracy of around 0.2% in $\lg V_g^0$, while that of the linear equation (2) is 0.8%. Thus the linear approximation provides quite satisfactory accuracy, and can be used in gas–liquid chromatography for various calculations and correlations, including the calculation of thermodynamic functions from retention indices.

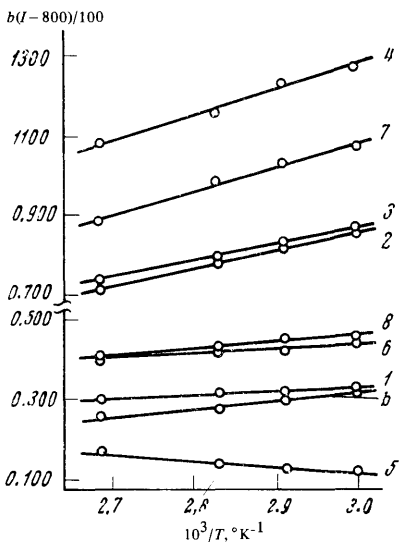


Figure 2. Dependence of $b(I - 800)/100$ on reciprocal of the temperature for the phase PEG-1000 [20] and the compounds: 1) $(C_2H_5)_2S$; 2) $(n\text{-}C_3H_7)_2S$; 3) $(CH_3S)_2$; 4) $(C_2H_5S)_2$; 5) $n\text{-}C_3H_7SH$; 6) $n\text{-}C_4H_9SH$; 7) $n\text{-}C_6H_{13}SH$; 8) C_6H_6.

The accuracy with which thermodynamic characteristics can be calculated from retention indices has been estimated[17,251]. Mathematical statistics have been used to deduce formulae for the standard deviation of the determination of thermodynamic functions by means of Eqns. (23)–(26) and (35–39). The accuracy of the calculation is comparable with that for the calculation of the same functions from specific retention volumes. Other work[243,252] has shown the fundamental possibility of determining thermodynamic functions from retention indices by extrapolation and interpolation.

Thus both experimental and theoretical results indicate that, among the gas-chromatographic retention parameters that are currently available, the system of indices is most generally applicable, is highly accurate and reproducible, and provides adequate information on stationary phases and chromatographic columns. The system of retention indices has a great advantage in analyses with programming of the temperature or the velocity of the carrier gas, as well as when high pressures are used. It is convenient also for the calculation of physicochemical quantities characterising the process of sorption in gas chromatography.

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Institute of Organoelementary Compounds,
USSR Academy of Sciences,
Moscow

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Group Identification of Hydrocarbons by Reaction Gas-chromatography

E.E.Kugucheva and A.V.Alekseeva

Methods for the group identification of hydrocarbons of the following classes have been examined: paraffins, olefins, conjugated dienes, acetylenes, naphthenes, and aromatic hydrocarbons. Methods of consecutive group analysis of complex industrial mixtures have been specially considered.
The bibliography includes 118 references.

CONTENTS

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I. CLASSIFICATION OF CHEMICAL-CHROMATOGRAPHIC METHODS OF ANALYSIS

The use of chemical reactions specific to substances with a particular functional group greatly simplifies the identification of the components of mixtures analysed by gas-chromatography. Therefore, soon after the publication of substances, studies were made where chemical reactions were employed for identification in gas-chromatography. Up to 1960 there were only a few studies of this kind: bromination was employed to determine multiple bonds[2], alcohols were determined with the aid of 3,5-dinitrobenzoyl chloride or acetic anhydride, and carbonyl compounds were determined by treatment with semicarbazide or 2,4-dinitrophenylhydrazine[3]. The structures of involatile organic compounds were established by preliminary pyrolytic[4] or oxidative decomposition[5].

Since 1960 the combination of the two methods of analysis has greatly developed and more than a thousand original studies and a number of reviews and monographs[6-13] dealing with methods of identification based on the results of chemical and chromatographic analyses have now been published.

Drawert et al.[14] were the first to combine in a separate group the methods of chromatographic analysis in which a reactor is placed in the carrier gas system of the chromatograph and which they called "reaction gas-chromatography".

Despite the recognition of Drawert's term by other authors of original studies and reviews[7-10], there is no complete unanimity concerning terminology. Thus methods in which a transformation of the specimen is combined with chromatographic separation have been included in reaction gas-chromatography in some reviews[6,11,12] regardless of the analytical procedure.

"Elimination" or "subtraction" methods, "transformation" or "peak shift" methods, as well as analytical methods which do not give rise to changes in the chromatogram can be distinguished on the basis of the changes in the chromatogram after chemical or physical modification of the specimen.

"Subtraction" or "elimination" consist in the conversion of compounds of a particular chemical type into involatile or undetectable products. The peaks corresponding to these transformed substances disappear (are "subtracted") in the chromatogram beyond the reactor. This method of identification was employed for the first time by Martin[15], who absorbed olefins in a reactor with sulphuric acid.

"Transformation" or "peak shift" are distinguished by the fact that the disappearance of the peaks from the chromatogram after treatment with the reagent is accompanied by the appearance of new peaks due to volatile reaction products. The term "peak shift" was employed for the first time by Langer and Pantages[16], who described the conversion of alcohols into trimethylsilyl ethers in the presence of hydrocarbons.

When the reactions are carried out after chromatographic analysis, there are no changes in the initial chromatograms. An example of this kind is provided by the qualitative group tests carried out at the instant of isolation of the substance from the chromatograph[17,18].

This review deals with methods for the analysis of hydrocarbons combining chromatographic separation with chemical and physicochemical processes, which lead to a change in the composition of the sample. Special identification procedures, such as pyrolysis and elemental analysis, have been excluded from consideration. Regardless of the experimental technique employed (using a divided or continuous scheme), the analytical methods have been grouped on the basis of the changes induced in the chromatogram after the transformation of the specimen. "Elimination" or "subtraction" methods are considered first and then the "transformation" or "peak shift" methods. Apart from the analytical methods applicable exclusively to hydrocarbons, methods of identification developed for mixtures of different classes of compounds, including hydrocarbons, are also quoted. Consecutive group analysis is treated separately, since this has become particularly important recently in the petrochemical industry.

II. "SUBTRACTION" OR "ELIMINATION" METHODS

"Subtraction" methods are most suitable for the group identification of complex mixtures, since in the assessment of the changes in the chromatograms after the transformation of a specimen the interpretation of the results is not complicated by the appearance of new peaks due to reaction products. A general disadvantage of the "subtraction" methods consists in the low accuracy of the

analysis at low concentrations of the components constituting the unresolved peaks.

1. Overall Determination of Unsaturated Hydrocarbons

Martin[15] was the first to employ an absorber with sulphuric acid in a single system with chromatographic separation and tested the effect of the reagent on model C_3–C_6 hydrocarbon mixtures. Sulphuric acid (98%) was deposited on silica gel in proportions of 3 : 2 by weight. The height of the reagent layer (2 cm) was sufficient for the quantitative absorption of unsaturated hydrocarbons of all classes, except ethylene, acetylene, and benzene. In order to remove ethylene and acetylene, it was necessary to add silver sulphate to sulphuric acid. A mixture of hydrocarbons could be analysed in two ways: either by comparing the chromatograms recorded before and after the reactor or by single-stage chromatography on apparatus with two katharometers and a reactor with sulphuric acid placed between them. The first detector recorded all the components of the initial mixture and the second only paraffins and naphthenes. The error of the method in the group determination of olefins amounted to 2–9%.

The reagent (98% sulphuric acid) has been used most widely in the gas-chromatographic analysis of petroleum fractions and of pyrolytic petrol[19–22].

Hines and Smith[19] employed sulphonation and dehydrogenation in a divided system with chromatographic separation for the group analysis of a petroleum fraction containing aromatic hydrocarbons, naphthenes, and paraffins. After the first sulphonation in order to remove aromatic hydrocarbons, the residue was subjected to dehydrocyclisation and the dehydrogenated product was again sulphonated. At each stage of the treatment the reaction product was chromatographed on a capillary column with squalane and the changes which had occurred in the mixture composition were inferred from the chromatograms.

Sulphuric acid at different concentrations was employed for the successive removal of unsaturated hydrocarbons of different classes[22]. Initially olefins were adsorbed with 80% sulphuric acid and then aromatic hydrocarbons with 98% sulphuric acid. The fraction of unsaturated hydrocarbons of each class was determined by comparing chromatograms obtained on a column with Apiezon L without complete separation of the components.

In the group analysis of petrols described below, Rowan[23] employed a reactor with sulphuric acid deposited on glass fibres. He noted that the absorption of olefins is accompanied by the evolution from the acid of hydrocarbons, which he did not identify.

Similar observations were made in another study[24]. In the absorption of olefinic admixtures in ethylene , an increase of the height of the isobutane peaks was observed together with the appearance of peaks due to new substances, which had been absent from the initial mixtures. The above investigators[23,24] did not consider the mechanism of the formation of new substances as a result of reaction.

Ipat'ev[25], who carried out a special investigation of the action of sulphuric acid on olefins, made the following important remark: "The determination of olefins with the aid of sulphuric acid in the presence of paraffins and naphthenes must be performed with caution using an excess of the acid and over a short period, since, on standing, olefin polymers which are sparingly soluble in sulphuric acid with the $d = 1.86$ are separated from it".

It is noteworthy that, in contact with sulphuric acid under optimal conditions (10–50°C), paraffins containing a tertiary carbon atom can also isomerise[26].

A novel location for the reactor with sulphuric acid in the chromatograph detector was proposed by Berezkin et al.[27] They placed the absorber between two katharometer chambers. A mixture of hydrogen and paraffins was not recorded by the detector, since the signals of the sensor elements cancelled out and the overall signal was proportional to the concentration of the olefin. Thus the concentration of olefins in a mixture with paraffins was established from a single chromatogram and not by comparing two chromatograms.

In the identification of atmospheric impurities, Williams[28] employed an absorber with sulphuric acid, deposited on Chromosorb in proportions of 1 : 4, designed for the absorption of unsaturated hydrocarbons. The impurities concentrated from air were either passed directly through the analytical column or through the absorber.

A separate investigation of the absorption properties of sulphuric acid at different concentrations was undertaken by Innes et al.[29], who found that, when the acid is diluted to 80%, the absorption of olefins became incomplete and at a concentration of 60% ceased completely.

Table 1. Absorption of hydrocarbons by chemical absorbents[29].

Hydrocarbon	Degree of absorption, %					
	20% $HgSO_4$ in 20% H_2SO_4	$Hg(CH_3COO)_2$	4% Ag_2SO_4 in 95% H_2SO_4	H_2SO_4		
				95%	80%	60%
Methane	0	0	0	0	0	0
Ethane	0	0	0	0	0	0
Propane	0	0	0	0	0	0
n-Butane	0	0	0	0	0	0
n-Hexane	0	0	0	0	0	0
n-Octane	0	0	0	0	0	0
Cyclohexane	0	0	0	0	0	0
Ethylene	100	94	100	11	6	0
Propene	100	100	100	100	67	0
Isobutene	100	100	100	100	100	100
Pent-2-ene	100	67	100	100	88	0
Hex-3-ene	100	60	100	100	85	0
4-Methylcyclohexene	100	70	100	100	70	0
Benzene	5	46	100	94	32	13
Toluene	0	22	100	100	33	0
p-Xylene	0	0	100	100	0	0
Acetylene	100	100	100	16	11	0

Apart from sulphuric acid, Innes et al.[29] investigated the absorption properties of a number of other reagents. They noted that liquid absorbers are less active than those deposited on a solid carrier. They prepared absorbers 10 cm long containing diatomaceous earth impregnated with liquid reagents and compared the degrees of absorption of hydrocarbons of different classes present in air at a concentration of 0.5% and contained in a sample having a volume of 5 ml (Table 1). Table 1 shows that mercury sulphate removed olefins quantitatively, while sulphuric acid with added silver sulphate eliminated in addition aromatic hydrocarbons. However, the latter reagent suffered from the disadvantage that ethylene was evolved for a long time after its absorption. The authors also established that nitric and hydrochloric acids and bromine water are ineffective. On the basis of their

investigation, they recommended that mercury sulphate be employed for the removal of olefins in gas-chromatographic analysis[30,31]. They developed a model of an industrial exhaust gas analyser[30], which consists of a chromatograph with two parallel columns and two flame-ionisation detectors with a reactor containing mercury sulphate placed in front of one of the columns.

It has been found[24] that the rate of reaction of olefins with mercury sulphate depends on the steric configuration of the olefins. The reaction is greatly retarded for the *trans*-isomers of β-olefins and fails to reach completion under the conditions of the stream of carrier gas.

In the chromatographic analysis of petrols[23,32,33] and exhaust gases[34], mercury perchlorate deposited on a solid carrier was also employed. This reagent absorbed olefins and partly aromatic hydrocarbons. For a quantitative elimination of aromatic hydrocarbons, it was necessary to add perchloric acid to mercury perchlorate. However, this led to the retention of branched paraffins in the absorber. The use of this reagent required special precautions. At room temperature high-boiling components were strongly absorbed, while on heating above 65°C the olefins were incompletely absorbed and side reactions with unsaturated hydrocarbons took place to a greater extent.

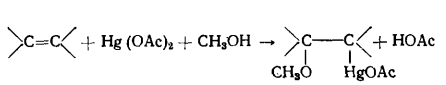
Albert[33] placed the absorber in the thermostat of the chromatogram in front of the analytical column and recommended that the absorber be back-flushed after each analysis in order to avoid the access of side products into the column in subsequent analyses.

Soulages and Briewa[35] investigated the interaction of olefins and aromatic hydrocarbons with mercury perchlorate. They found that the degree of reaction in the absence of side processes depends on the extent to which the optimal conditions are maintained: the amount of absorbent, the contact time, temperature, and the moisture content of the carrier gas. The last factor is particularly important. The moisture content in the gas must be equivalent to the vapour pressure of the absorbent; only then does the concentration of perchloric acid remain constant. Since in previous investigations the moisture content of the gas was not taken into account, dilution or increase of the acid concentration might have been a likely source of secondary phenomena.

It has been suggested that an absorber with mercury perchlorate be employed for the type analysis of liquid industrial mixtures. Analytical schemes[35-37] are discussed below.

Kerr and Trotman-Dickenson[38] suggested that a paste of mercury acetate and nitrate in ethylene glycol deposited on a refractory brick be used to absorb olefins under flow conditions.

Doring and Hauthal[39] investigated the kinetics of the competing reaction of olefins with mercury acetate in methanol:



They established that the rate of esterification with mercury acetate decreases in a series of olefins with different structures in the following proportions: α-olefins: β-olefins: γ-olefins = 100 : 10 : 1, *cis*-isomers reacting faster than their *trans*-analogues. In order to identify C_6–C_8 olefins, the authors removed samples from the reaction mixture at different times after the start of the reaction and subjected them to chromatographic analysis. The degree of conversion of the unknown component was calculated from the decrease of its peak height and its structure was established.

As already noted earlier, Innes et al.[29] found that bromine water is ineffective for the absorption of olefins under flow conditions. However, bromination in a stream has been carried out with bromine deposited on activated charcoal, which was capable of the stable retention of up to 40 wt.% of bromine. Wirth[40] achieved a quantitative separation of a mixture of ethylene, acetylene, and ethane. At −78°C only ethylene reacted with the bromine and at 0°C acetylene reacted as well. The gases which failed to react were desorbed with evacuation, and were collected in a measuring burette. Ray[41] used this method to establish the content of light impurities in ethylene. Ethylene was brominated at room temperature. Non-olefinic impurities were removed from the charcoal column in a stream of carbon dioxide and were collected in a nitrometer over aqueous alkali.

Bromination under flow conditions was carried out separately from the subsequent chromatographic analysis in some investigations[24,42]. In order to reduce the volatility of bromine, its solution in aqueous sodium bromide was employed. The reagent, deposited on Chromosorb in proportions of 1 : 1 by weight, eliminated quantitatively olefins and C_2–C_8 dienes from vapour–gas mixtures.

Hoff and Feit[43] used a saturated solution of bromine water under static conditions to absorb the vapours of olefins and certain oxygen-containing compounds.

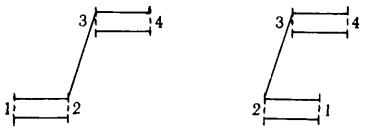
In this section of the review, it is useful to consider the analytical method described by James and Martin[2] and Hoff and Feit[43]. Although aliphatic acids and not hydrocarbons were the object of investigation, this procedure may be of wider applicability. The authors brominated the methyl esters of saturated and unsaturated aliphatic acids in the liquid phase and compared the chromatograms of the initial mixture and the reaction products. James and Martin[2] carried out the chromatographic separation of such products on Apiezon L as the stationary phase. By subtracting the peaks of the bromides of the unsaturated components, they were able to distinguish the esters of acids of two types—saturated and unsaturated. Landown and Lipski[44] improved this method by using for the separation a more polar phase—diethylene glycol glutarate. After bromination, the peaks due to the dibromides (which the authors identified component by component) were seen on the chromatograms obtained with the aid of this phase, in addition to the peaks due to the saturated acid esters. Thus they established that the esters belonged to three groups of compounds: (1) saturated compounds whose peaks remained unchanged under bromination; (2) mono-olefins the disappearance of whose peaks was accompanied by the appearance of those of the dibromides; (3) polyolefins the removal of which after bromination did not entail the appearance of the peaks of the corresponding tetra- and hexa-bromides owing to the low vapour pressures of the latter.

2. Identification of Conjugated Dienes and Acetylenes

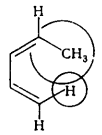
Janak and Novak[45,46] used maleic anhydride to retain the main mixture component (butadiene) and to determine in the latter the admixtures of light hydrocarbons. Maleic anhydride deposited on Kieselguhr was placed in the reactor in front of the analytical column. The authors noted the following disadvantages of the method: solubility

of light hydrocarbons in maleic anhydride and the catalytic effect of traces of maleic acid on the polymerisation of isobutene. The degree of absorption of butadiene increased with catalyst temperature and it was difficult to maintain the optimal temperature because the anhydride sublimed readily and blocked the gas channels in the apparatus.

The reactivity of dienes in Diels–Alder reactions depends on the structure, configuration, and the nature of substituents in the conjugation chain [47]. In the two possible coplanar systems [(I) and (II)], the reacting 1,4-carbon atoms approach one another sufficiently closely for diene condensation only in dienes with a cisoid disposition of the carbon bonds [system (II)]:

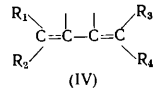


The transoid conformation (I) is characteristic of the *cis*-piperylene molecule. In the cisoid form (III) the distance between CH_3 and H would be less than the sum of the van der Waals radii of these groups. This would lead to a considerable internal strain, as a result of which the cisoid conformation is hindered.



(III)

Dienes with fully substituted terminal C atoms of the conjugated system (IV) are likewise incapable of undergoing the Diels–Alder reaction.



(IV)

Gil-Av and Herzberg-Minzly [48,49] investigated by gas chromatography the kinetics of the reaction of dienes with chloromaleic anhydride. They employed chloromaleic anhydride as the stationary phase and chromatographed the mixture of dienes at different flow rates of the carrier gas. Since in the presence of an excess of anhydride the reaction became pseudomonomolecular, its rate was directly proportional to the contact time. Therefore the decrease of the peak areas for dienes with the cisoid conformation, reacting with the anhydride [47], depended on the flow rate of the carrier gas, while for other dienes the peak areas remained constant. The authors employed these findings for the identification of dienes [48]. *cis*- and *trans*-Piperylenes and 2,4-hexadienes were identified in this way.

Berezkin and coworkers [50–52] also made a chromatographic study of the kinetics of the reactions of dienes with maleic anhydride. In order to increase the temperature and the contact time, the reagent (maleic anhydride) was introduced in solution in tricresyl phosphate. The reactor with the anhydride was placed between two detectors. In each analysis the concentrations of the diene before and after absorption were obtained. The authors suggested that this method be used to calculate the rate constants for bimolecular reactions at variable concentrations of the anhydride. In addition, the method may be useful in the determination of the initial concentrations of unstable compounds [52]. It has been shown for butadiene that the error of the method is 3–4 rel.%.

Kugucheva and Alekseeva [24,53] used the reaction with maleic anhydride to identify the dienes present in vapour–gas mixtures in microconcentrations. The analytical scheme with separate steps made it possible to raise the reactor temperature to 135°C and to increase sharply the absorption of dienes (Table 2).

Table 2. Absorption of hydrocarbons by maleic anhydride [53].

Hydrocarbon	Degree of absorption, mole %	Hydrocarbon	Degree of absorption, mole %
Butadiene	73	*cis*-Penta-1,3-diene	26
Isoprene	100	Cyclopentadiene	100
trans-Penta-1,3-diene	90	2,3-Dimethylbuta-1,3-diene	100

Together with a high degree of absorption of dienes, an enhanced solubility of compounds, non-specific in relation to the reagents, was noted [24].

An aqueous solution of silver nitrate deposited on Chromosorb has been used [53] to absorb monosubstituted acetylenes. The reaction was quantitative and was not complicated by secondary phenomena.

3. Adsorption of n-Alkanes on a 5 Å Molecular Sieve

Molecular-sieve analysis in gas chromatography was achieved for the first time by Brenner and Coates [55]. They placed the reactor with the 5 Å molecular sieve in front of the analytical column and showed that n-alkanes in a mixture of C_3–C_{11} straight-chains and branched-chain alkanes, cycloalkanes, and aromatic hydrocarbons were retained in the reactor at 60–180°C.

Adlard and Whitham [56] compared the results of liquid-phase and vapour-phase adsorption of n-alkanes on a 5 Å molecular sieve and the results of extraction by urea and obtained similar results. They extended the molecular sieve analysis in chromatography to hydrocarbons with up to 44 carbon atoms [56–58]. In order to prevent the spreading of the chromatographic peaks when the specimen passes through the reactor, the zeolite was impregnated with a small amount of the stationary phase.

Barrall and Baumann [59] investigated the effect of water remaining in the zeolite pores on the accuracy of the molecular-sieve analysis in chromatography. They found that traces of water cause degradation of the zeolite pores, which leads to the breakthrough of the straight-chain hydrocarbons during analysis and a rapid decrease of the adsorption capacity of the sorbent. High-temperature dehydration procedures under various conditions have been proposed for the activation of zeolites: by evacuation [60], in a stream of nitrogen or helium [61], and in an open system [62]. Dehydration by heating to 350–400°C in a stream of dry nitrogen is most frequently employed.

Molecular-sieve analysis in gas chromatography is widely employed in group determination of n-alkanes in petrols, kerosenes, and waxes [23,33,63].

In the determination of small amounts of n-alkanes in a mixture with branched-chain alkanes, Eggertsen and Groennings [63] placed two reactors in the anlytical circuit.

The first analytical cycle included separation on the chromatographic column, absorption of n-alkanes in the reactor with the zeolite placed beyond the analytical column, and the recording of the residual branched-chain alkanes by the katharometer. In the second cycle the n-alkanes retained in the reactor were desorbed and were redirected with the aid of the back-flushing apparatus to the analytical column. In the course of their elution from the column, the n-alkanes entered the second reactor where they were combusted to carbon dioxide and were recorded by the katharometer with a higher sensitivity than the initial alkanes. The method permitted the determination of n-alkanes at concentrations down to 0.01% and branched-chain alkanes present in large amounts did not interfere.

In the first study involving the application of a 5 Å molecular sieve in gas-chromatographic analysis, Brenner and Coates [55] already mentioned the possibility of extending their analytical procedure to compounds of other homologous series. Subsequently they demonstrated for artificial mixtures of hydrocarbons and oxygen- and halogen-containing compounds that straight-chain olefins, alcohols, acids, and aldehydes are also retained in the zeolite pores [69].

However, molecular sieve analysis has not been widely used in the study of compounds belonging to classes other than the paraffins owing to the aluminosilicate catalytic activity of the zeolite [54, 70].

Table 3. Isomerisation of olefins on contact with a Linde molecular sieve at 200°C. [75]

Initial substance	Reaction products		Degree of reduction*
	hydrocarbons	content, %	
2-Methylbut-1-ene	2-Methylbut-1-ene	29	71
	2-Methylbut-2-ene	71	
2-Methylpent-1-ene	2-Methylpent-1-ene	24	76
	2-Methylpent-2-ene	76	
2,3-Dimethylbut-1-ene	2,3-Dimethylbut-1-ene	25	75
	2,3-Dimethylbut-2-ene	75	
2,3-Dimethylbut-2-ene	2,3-Dimethylbut-1-ene	25	75
	2,3-Dimethylbut-2-ene	75	
trans-3-Methylpent-2-ene	*trans*-3-Methylpent-2-ene	60	40
	cis-3-Methylpent-2-ene	34	
	2-Ethylbut-1-ene	6	
cis-3-Methylpent-2-ene	*trans*-3-Methylpent-2-ene	60	
	cis-3-Methylpent-2-ene	34	66
	2-Ethylbut-1-ene	6	
2,3,3-Trimethylbut-1-ene	2,3,3,-Trimethylbut-1-ene	100	0

*Calculated relative to the isomerisation products.

There are only isolated reports on the molecular sieve analysis of olefins in gas chromatography [59, 67, 69]. This is due to the isomerisation of straight-chain olefins during their desorption [56, 71, 72]. There are also data indicating the isomerisation of iso-olefins on contact with the zeolite [73].

However, there exist contradictory views concerning the nature of the isomerisation of olefins. Norton [74], who characterised the isomerising properties of zeolites of various types, concluded that a 5 Å molecular sieve is inactive in relation to olefins. On the other hand, Baas and Vlugter [73] not only observed the migration of the double bond in the molecular under these conditions but also skeletal isomerisation.

Kugucheva and Aleksseva [75] investigated the behaviour of individual isomeric olefins on contact with a zeolite under flow conditions. Branched-chain olefins did indeed change: instead of a single peak on the initial chromatogram, two or three peaks appeared beyond the reactor. For the olefins listed in Table 3, the transformations consisted in the migration of the double bond and in a change of the steric configuration. There was no skeletal isomerisation, which was specially confirmed in relation to 2,3,3-trimethylbut-1-ene. The migration of the double bond in the molecule of this isomer is impossible due to the presence of the quaternary carbon atom. The results of chromatographic analysis beyond the catalyst with the zeolite confirmed the absence of isomerisation.

Investigators [64, 66, 75] who used low concentrations of various substances noted that a certain amount of compounds having a critical molecular diameter greater than the pore size of the molecular sieve (5 Å) undergoes irreversible absorption on contact with the zeolite, namely cycloalkanes, branched-chain alkanes or aromatic hydrocarbons. This adsorption is not eliminated when the zeolite is impregnated with a small amount of the stationary phase [66]. The reason for the absorption may be adsorption on the outer surface of the zeolite crystals and, in the case of zeolite granulated with a binder, on the surface of the secondary pores formed by the gaps between the zeolite crystals and the coarse-grained binder [76, 77]. The possibility of methyl-substituted alkanes being able to pass into the molecular sieve pores as a result of a change in the pore size and in the critical diameter of the hydrocarbon molecules at a high temperature has been examined [78].

III. "TRANSFORMATION" OR "PEAK SHIFT" METHODS

1. Exhaustive Hydrogenation of Unsaturated Hydrocarbons

The elimination method, a great advantage of which is simplicity of the interpretation of the chromatograms, are of limited applicability because it is possible to make only a group identification of the components of the mixture analysed, involving their assignment to groups of substances which react in the same way with the reagent employed. In the case of hydrogenation, on the other hand, which is one of the transformation methods where the chromatogram shows, instead of the peaks of the initial unsaturated hydrocarbons, those of the saturated analogues, there is a possibility of "skeletal" identification, i.e. one can determine the hydrocarbon skeleton of the initial molecule. However, the positions of the multiple bonds and the *cis–trans* configuration of the olefins remain unknown.

Moreover, in contrast to the elimination method, the reduction method can yield information about the composition of the unresolved peaks corresponding to several unsaturated hydrocarbons. In this case "elimination" makes it possible to infer the presence of multiple bonds in the molecules and hydrogenation can achieve the separate identification of the components in terms of their saturated analogues.

Reduction usually leads to a simplification of the composition of mixtures and to a more complete chromatographic separation. The method has been widely used in the gas-chromatographic analysis of petroleum fractions.

In one of the first studies on the chemical-chromatographic analysis of petroleum, Nelson et al. [79] used a

multistep analytical scheme in which each step was carried out separately. In the first step saturated hydrocarbons were separated by liquid-phase chromatography on silica gel. Paraffins and naphthenes in the isolated fraction were identified component by component. The identification was carried out with the mixture separated on columns with two stationary phases of different polarity—squalane and silicone oil, using a standard mixture of isomers. The corresponding paraffin and naphthene peaks were found on the chromatogram of the initial mixture before the separation on silica gel. After the liquid-phase reduction of the initial mixture in the presence of palladium on charcoal (10% Pd) at 100°C, the content of olefins and their hydrocarbon skeletons were determined from the increments in the peak areas of the known paraffins and naphthenes. The authors estimate the error of the method as ±6%.

Hydrogenation in a microreactor in a stream of hydrogen, which serves at the same time as the carrier gas in the apparatus, has been widely used. The reactor is placed in front of the sample inlet or in front of the analytical column. The advantage of the process carried out in this way consists in a very rapid reaction and a very low consumption of the catalyst, the activity of which hardly changes owing to the small sample volume. Group VIII metals on various carriers have been used as catalysts.

Klesment et al.[80] investigated the properties of catalyst carriers employed for reduction in chromatographic analysis. They found that alumina gives rise to side reactions involving cracking, isomerisation, and cyclisation and activated charcoal and silica gel adsorb organic compounds too strongly. The authors employed platinised diatomaceous earth (2–10% Pt) saturated with hydrogen as the catalyst. The petrol specimens from shale oil which they employed were reduced in a microreactor at 200°C in a stream of hydrogen or helium and were then transferred to the analytical column.

Rowan[23] suggested that olefinic and aromatic hydrocarbons be hydrogenated on a platinum catalyst (Pt/Al_2O_3) at 299°C and that the selective reduction of olefins alone be performed on a palladium catalyst (5% Pd on asbestos) at room temperature.

Nickel, platinum, and palladium catalysts have been used for the vapour-phase hydrogenation and investigation of the composition of shale petrols[81–83] and other petroleum products[21,84,85], including procedures where hydrogenation was combined with pyrolysis[86,87].

An interesting combination of reduction reactions with separation of the products on a capillary column was proposed by Struppe[88]. An aluminium capillary 6 m long with an internal diameter of 0.3 mm was filled with chloroplatinic acid, which was reduced in a stream of hydrogen at 150°C. Platinum black was then deposited on the inner walls of the capillary. The capillary reactor thus obtained was placed between the sample inlet and the separating column. Mono-olefins, dienes, and cyclo-olefins were reduced in the reactor at 125°C. Aromatic hydrocarbons and naphthenes did not react. Individual identification could be achieved by combining the reactor with capillary columns filled with different stationary phases. The author determined the time required by the sample to pass through the capillary reactor and took it into account in the calculation of the retention volumes.

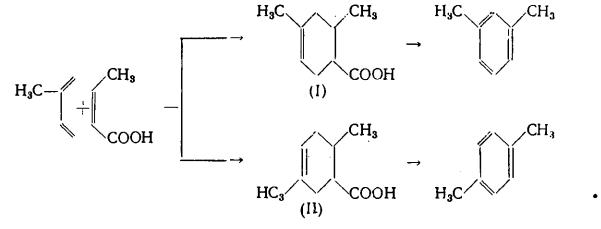
The method involving the reduction of individual compounds of different classes, including unsaturated hydrocarbons, has been investigated systematically by Beroza and coworkers[10,89,90]. The authors developed a model of a standard apparatus for hydrogenation[90], which can be connected to any chromatograph with a katharometer or a flame-ionisation detector. The gas channel scheme was such that the reaction products were transferred by the carrier gas directly to the analytical column. The reduction was carried out on a palladium catalyst (1% Pd on Gas Chrom P) at different temperatures and hydrogen flow rates. Table 4 summarises the results of hydrogenation under conditions leading to the formation of the hydrocarbon with the same number of carbon atoms as in the initial compounds or to a lower homologue.

Table 4. Determination of the carbon skeleton by hydrogenation using Beroza's method[10] (catalyst—1% Pd on Gas Chrom P, temperature 300°C, hydrogen flow rate 20 ml min^{-1}).

Classes of substances yielding a hydrocarbon analogue	Reaction
Paraffins	None
Unsaturated hydrocarbons	Hydrogenation of double bond
Halogeno-derivatives	Dissociation of C–X bond
Secondary and tertiary alcohols	Dissociation of C–O bond
Secondary and tertiary ethers	Dissociation of C–O bond
Ketones	Dissociation of C=O bond
Secondary and tertiary amines	Dissociation of C–N bond
Amides (amine component with a secondary or tertiary carbon atom)	Dissociation of C–N bond
Classes of substances yielding a hydrocarbon analogue and (or) the next lower hydrocarbon homologue	**Reaction**
Aldehydes	$RCHO \rightarrow RH,\ RCH_3^{\alpha}$
Acids	$RCOOH \rightarrow RH,\ RCH_3^{\alpha}$
Anhydrides	$(RCO)_2O \rightarrow RH,\ RCH_3^{\alpha}$
Primary alcohols	$RCH_2OH \rightarrow RH,\ RCH_3^{\alpha}$
Esters, alcoholic component with a primary carbon atom (OCH_2R) and R'CO acid component	$R'COOCH_2R \rightarrow RH,\ RCH_3$; $R'H,\ RCH_3^{\alpha}$
Primary ethers	$RCH_2OCH_2R \rightarrow RH, RCH_3$
Amides, amine component ($NHCH_2R$) at a primary carbon atom, R'CO acid component	$R'CONHCH_2R \rightarrow RH,\ RCH_3$; $R'H,\ R'CH_3^{\alpha}$

*α—slight or none.

The practical application of the method can be clearly demonstrated using as an example the reaction of isoprene with crotonic acid[10]:



In order to identify the product formed in the reaction [(I) or (II)], it was reduced at 330°C. Apart from decarboxylation, the aromatic ring underwent aromatisation at this temperature. *m*-Xylene, corresponding to reaction product (I), was identified on the basis of the retention time. The identification was confirmed by the ultraviolet spectrum. The usual methods for the determination of structure by an oxidation procedure would have been more laborious.

In reduction by Beroza's method, it is necessary to maintain the hydrogenation conditions exactly, since at temperatures intermediate between the optimal values (200°C for hydrogenation and 300°C for dehydrogenation), alicyclic and aromatic derivatives are formed in different proportions.

The reduction is usually accompanied by the formation of intermediates or side products. Beroza [91] suggested, for example, that ketones be identified not only on the basis of the main product of the hydrogenation reaction (the hydrocarbon analogue) but also on the basis of the small amounts of compounds appearing as a result of the dissociation of the bond between the carbon atom and the adjacent carbonyl group. Thus ethane and butane were detected in the reduction of 3-heptanone in addition to n-heptane.

It is difficult to carry out the hydrogenation reaction in a single cycle with chromatographic separation because of the spreading of the chromatographic peaks and the change in the retention times of the components on passing through the reactor. This is caused by adsorption on the catalyst layer and occurs to a particularly marked extent in the analysis of polar or high-boiling substances.

Beroza [10] suggested that, in order to establish the structure of the hydrocarbon skeleton of strongly adsorbed compounds, one should collect initially the reduction products in a cooled trap and then introduce them into the chromatograph.

Langner [92] investigated the influence of various methods of packing of the catalyst in the reactor on the retention times of substances reduced by Beroza's method. He found that the retention times change after filling the reactor with a fresh portion of the catalyst. In order to obtain reproducible relative retention times, it is necessary to carry out a calibration with standard substances directly before or after the analysis.

Even in the reduction of pure substances, the nature of the test substance must be known for a correct interpretation of the results. For example, different chemical compounds such as toluene, benzyl alcohol, benzaldehyde, and benzonitrile give rise to the same product on reduction–methylcyclohexane.

An interesting method for determining the chemical nature of the test substance in the reduction process was proposed by Franc and Kolouskova [93], who investigated the relation between the number of reduced double bonds or the functional group and the ratio of the retention times of the initial and reduced compounds. They found that the logarithm of the ratio of the retention volumes of the corresponding analogues is determined solely by the type of functional group. On the basis of their relation, they identified hydrocarbons and other compounds. They designed a special device for analysis whereby it is possible to record in a single chromatographic cycle both the initial and the reduced compounds. An empty glass capillary was inserted through the reactor containing a platinum catalyst (10% Pt on pumice). The sample introduced was divided in the reactor into two parts. One part passed through the capillary to the analytical column in an unchanged form and the other was reduced on contact with the catalyst.

2. Selective Hydrogenation of Conjugated Dienes and Acetylenes

Beroza and Sarmiento [90], who investigated the reduction of unsaturated acids esters with different numbers of double bonds in different positions, attempted to relate the change in the retention time of the reduced compound to the position of the double bond. By reducing the contact time with the catalyst, they identified the incomplete reduction products on the chromatogram. However, according to their data, the interpretation of the chromatograms did not always lead to unambiguous results and was not developed further in subsequent investigations.

A more successful attempt to employ partial reduction for identification was made by Smith and Ohlson [94]. The pure substances or narrow fractions were isolated on a preparative scale, collected in a U-shaped reactor, and hydrogenated on the Adams catalyst (PtO_2 with added iron) or sodamide. After raising the temperature, hydrogen was passed into the reactor at a pressure of 3 atm and the system was maintained at 80–90°C for 1 min in order to complete the reduction process. After connecting the chromatograph to the device for the introduction of the sample, the volatile reaction product entered the analytical column.

Table 5. Hydrogenation of dienes on the Adams catalyst [94].

Initial hydrocarbon	Unchanged fraction	Composition of catalytic reaction mixture			
		partly reduced products	wt.%	fully reduced products	wt.%
Buta-1,3-diene	82	But-1-ene	6		
		cis-But-2-ene	1	n-Butane	9
		trans-But-2-ene	2		
Penta-1,4-diene	75	Pent-1-ene	9	n-Pentane	16
cis-Penta-1,3-diene	21	Pent-1-ene	4		
		cis-Pent-2-ene	10	n-Pentane	58
		trans-Pent-2-ene	7		
trans-Penta-1,3-diene	9	Pent-1-ene	4		
		cis-Pent-2-ene	3	n-Pentane	78
		trans-Pent-2-ene	6		
Penta-1,2-diene	98	Pent-1-ene	0.3		
		cis-Pent-2-ene	0.6	n-Pentane	1
		trans-Pent-2-ene	0.7		
Hexa-1,5-diene	68	Hex-1-ene	11	n-Hexane	21
cis, trans-Hexa-2,4-diene	22	*cis*-Hex-2-ene	8		
		trans-Hex-2-ene	14	n-Hexane	47
		cis-Hex-3-ene	3		
		trans-Hex-3-ene	6		
trans, trans-Hexa-2,4-diene	15	*cis*-Hex-2-ene	2		
		trans-Hex-2-ene	14	n-Hexane	60
		cis-Hex-3-ene	3		
		trans-Hex-3-ene	6		
trans-Hexa-1,3-diene	60	*cis*-Hex-2-ene	2	n-Hexane	20
		trans-Hex-2-ene	15		
		trnas-Hex-3-ene	3		
Cyclopenta-1,3-diene	79	Cyclopentene	8	Cyclopentane	13

On shortening the reaction time, the dienes and acetylenes were not reduced completely. The authors investigated the partial reduction products of certain dienes (Table 5) and acetylenes (Table 6) and suggested that the method be employed for their identification. Tables 5 and 6 show that the catalysts chosen by the authors are not very selective. The reduction either takes place to a very low degree or leads to completely hydrogenated products. The method requires a relatively high content of the components to be separated, which are detected by a katharometer, and is applicable only to pure compounds.

Kugucheva and Alekseeva [60,95] proposed a method for the identification of conjugated dienes and acetylenes mixed with hydrocarbons of other classes. The method consists in the selective reduction of dienes and acetylenes, olefins being involved in the reaction to only a slight extent.

Palladium prepared by Lindlar's method [96] was chosen as the catalyst. The hydrogenation was carried out under flow conditions at room temperature. The conjugated dienes and acetylenes with different structures and steric configurations were reduced to a high degree and selectively to olefins (Table 7). The olefins reacted (reduction and isomerisation) to an extent not greater than 20% (Table 8). The method, which was developed on artificial mixtures, was applied to real products of petrochemical synthesis [85].

Table 6. Hydrogenation of acetylenes [94].

Initial hydrocarbon	Catalyst	Unchanged fraction, %	Composition of catalytic reaction mixture			
			partly reduced products	wt.%	fully reduced products	wt.%
Hex-3-yne	PtO_2	50	*cis*-Hex-3-ene	15	n-Hexane	32
			trans-Hex-3-ene	3		
	$NaNH_2$	90	*trans*-Hex-3-ene	10	„ „	0
Hex-2-yne	PtO_2	55	*cis*-Hex-2-ene	10	„ „	33
			trans-Hex-2-ene	2		
	$NaNH_2$	60	*trans*-Hex-2-ene	40	„ „	traces
	PtO_2	96	Hex-1-ene	3	„ „	1
Hex-1-yne	$NaNH_2$	38	Hex-1-ene	62	„ „	0
	Na	37	Hept-1-ene	63	„ „	0

Table 7. Hydrogenation of dienes and acetylenes on a palladium catalyst [53].

Initial compound	Composition of catalytic reaction mixture		Degree of reaction, %
	hydrocarbon	mole %	
Buta-1,3-diene	n-Butane	3.1	100.0
	But-1-ene	51.3	
	trans-But-2-ene	40.2	
	cis-But-2-ene	5.4	
Isoprene	2-Methylbutane	4.3	100.0
	3-Methylbut-1-ene	21.1	
	2-Methylbut-1-ene	25.1	
	2-Methylbut-2-ene	49.5	
Penta-1,3-diene (70% of *trans*-form and 30% of *cis*-form)	n-Pentane	5.4	100.0
	Pent-1-ene	22.3	
	trans-Pent-2-ene	61.4	
	cis-Pent-2-ene	10.9	
Cyclopentadiene	Cyclopentane	14.9	100.0
	Cyclopentene	85.1	
Penta-1,4-diene	n-Pentane	7.9	51.2
	Pent-1-ene	34.7	
	trans-Pent-2-ene	7.2	
	cis-Pent-2-ene	0.4	
	Penta-1,4-diene	49.8	
Acetylene	Ethane	21.3	100.0
	Ethylene	78.7	
Hex-1-yne	n-Hexane	25.2	100.0
	Hex-1-ene	68.0	
	cis-Hex-2-ene	6.8	
Hex-2-yne	n-Hexane	1.1	8.77
	trans-Hex-2-ene	4.1	
	cis-Hex-2-ene	82.5	
	Hex-2-yne	12.3	

3. Dehydrogenation of Naphthenes

Keulemans and Voge [97] were the first to suggest the dehydrogenation of naphthenes in gas-chromatographic analysis. They were aromatised on a reforming catalyst (platinum on Al_2O_3 containing a halogen) at 350°C in a stream of hydrogen. The reaction products were transferred by the stream of hydrogen to the analytical column. The authors found that cyclohexane derivatives were aromatised to the extent of 96–100% except for the 1,1-dimethyl derivative (66%). Cyclopentanes were converted into benzene derivatives to the extent of only 1.4 to 25%.

Table 8. Reactions of olefins on a palladium catalyst [53].

Hydrocarbon	Degree of reaction, mole %		Hydrocarbon	Degree of reaction, mole %	
	hydrogenation	isomerisation		hydrogenation	isomerisation
Pent-1-ene	12.9	6.9	2-Methylbut-2-ene	0.0	0.0
Hex-1-ene	10.5	7.2	*trans*-Hex-2-ene	0.0	4.7
3-Methylbut-1-ene	0.0	0.0	Cyclopentene	5.3	—
2-Methylbut-1-ene	0.0	0.0			

In order to suppress the aromatisation of cyclopentane hydrocarbons, Rowan [23] carried out the dehydrogenation at 299°C in a stream of helium with a small amount of added hydrogen. Dehydrogenation, which takes place to the extent of 100% for six-membered naphthenes, was used as a method for their group identification in complex hydrocarbon mixtures.

Klesment et al. [80] dehydrogenated petrols in a stream of helium at 325°C on platinum black deposited on diatomaceous earth. The yield of aromatic hydrocarbons from six-membered naphthenes was 87% and above, while five-membered cycloalkanes did not react. The process was complicated by cracking. The catalytic aromatisation of naphthenes and heterocyclic compounds on platinium catalysts was also carried out by Nigam [98].

Ivanova et al. [99] aromatised by the Zelinskii method the fraction of paraffins and naphthenes isolated by liquid–liquid chromatography and deduced the results on the basis of subsequent gas-chromatographic analysis.

The dehydrogenation and sulphonation of the aromatisation products in a system with separate steps involving subsequent chromatographic separation [19] have already been described.

4. The Introduction of the Methylene Group

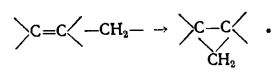
Dvoretzky et al. [100] treated alkanes, cycloalkanes, and olefins with diazomethane and then separated the reaction products on a capillary column with squalane. The treatment with diazomethane was accompanied by short-wavelength irradiation. In order to avoid side reactions between the methylated products and diazomethane, the reaction was carried out with a 50-fold excess of the hydrocarbon.

The methylene group is introduced according to the following scheme:

$$\rangle C{-}H + {-}CH_2{-} \rightarrow \left[\rangle C{-}CH_2{-}H\right] \rightarrow \rangle C{-}CH_3 .$$

This method of introduction is independent of the type of C–H bond: aliphatic vinyl, or allyl. The yield of isomers is directly proportional to the number of primary, secondary, and tertiary C–H bonds in the initial hydrocarbon molecule and can be calculated beforehand.

The reaction with olefins is complicated by the formation of cyclopropane:



The ratio of the contributions of the C=C/C–H reactions varies in the range from 6 to 8 and therefore the corresponding substituted cyclopropane is the main reaction product.

The method has been applied mainly to alkanes. The structure of the unknown component was established on the basis of the number and relative amounts of the methylenation reaction products. Moreover, data for the contents of the isomers obtained may be used to identify unknown mixtures. The retention times of 19 nonanes synthesised from 6 initial octanes have been obtained [101]. By comparing the retention times of the nonanes and the components of a real mixture—the products of the alkylation of isobutane with olefins—the authors determined the mixture composition.

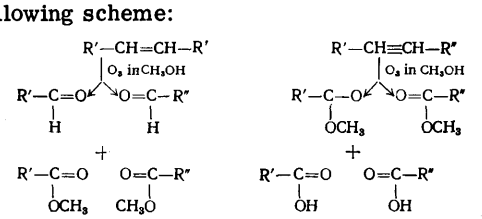
It has been shown for a large number of examples involving alkanes [100] that the ratio of the yields of the isomers coincides with theoretical predictions within the limits of the error of the chromatographic analysis.

5. Ozonolysis

Blumer and Thomas [102] isolated on a preparative scale the olefin fraction from a plankton extract and subjected it to ozonolysis. The ozonides were cleaved in the chromatograph injector and the presence of methylene and vinyl groups as well as conjugated double bonds in the molecule of the initial olefin was inferred on the basis of the identified carbonyl compounds.

Davison and Dutton [103] placed a reactor with zinc oxide beyond the chromatograph injector. Acidic compounds formed on decomposition of the ozonides were retained in the reactor, while aldehydes passed to the analytical column without hindrance.

Spencer et al. [104] used the ozonolysis method for the identification of double and triple bonds. They ozonised hydrocarbons in methanol solution. After subsequent cleavage of the ozonides (also carried out in the chromatograph injector), only olefins gave rise to aldehydes, while esters and acids were obtained from acetylenic hydrocarbons. The reaction was carried out according to the following scheme:



Thus 83% of methyl valerate and 17% of valeric acids were obtained from dec-2-yne, which was completely ozonised after 7 min.

Smith et al. [105] ozonised unsaturated compounds isolated by preparative chromatography. The carbonyl compounds obtained on decomposition of the ozonides were treated with dinitrophenylhydrazine. The dinitrophenylhydrazones isolated were identified by paper chromatography. The ozonolysis method has been used successfully to identify C_6–C_{11} α-olefins, C_5–C_6 dienes, styrene, pentynes, etc. Ozonolysis combined with gas chromatography has also been used in other investigations [106,107].

6. Other Identification Methods

Frank et al. [108] used reductive catalytic cleavage for the identification of alkyl substituents in the aromatic ring. The reaction was carried out at 620°C in a quartz tube filled with the Leuna WK 9063 catalyst (silicon and aluminium oxides in proportions of 60:40, impregnated with 4.5% WO_3 and MoO_3) in a stream of hydrogen, which served as the carrier gas in the apparatus. The reaction tube was connected to the sample injection device, so that the volatile cleavage products entered the analytical column directly. At the above temperature carbon–carbon bonds in the alkyl group were ruptured in all positions and the relative amounts of the hydrocarbons formed remained constant (to within ±3 rel.%). On the basis of the ratios of the reaction products obtained, it was possible to infer whether one or several alkyl groups are split off from the initial alkylbenzene. The authors also established that there are optimal temperatures for the scission of various alkyl groups and suggested that this phenomenon be employed for identification. 5-Isopropyl-1,2,4-trimethylbenzene gives rise to only propane at 200°C, to propane and propene at 300°C, to propane, propene, ethane, and ethylene at 500°C, and to methane as well as the compounds enumerated above at 600°C.

Walsh and Merrit [17] treated the elutate with reagents for qualitative analysis directly at the outlet from the column. A device for dividing the stream into five parts was connected to the outlet tube of the katharometer. This made it possible to carry out five calorimetric reactions for each substance. Reagents were proposed for oxygen-, sulphur-, nitrogen-, and halogen-containing compounds and also for aromatic hydrocarbons and olefins. Having determined the homologues series to which the compound belongs, it was identified with the aid of plots of the logarithm of the retention volume against the number of carbon atoms in the molecule.

Casu and Cavalotti [18] improved the method by suggesting an attachment to the pen recorder of the chromatograph. A glass strip on which a layer of silica gel impregnated with the appropriate reagents has been deposited, moves at the same speed as the paper strip of the pen recorder. A coloured spot appears on the silica gel synchronously with the appearance of a peak on the chromatogram.

The methods described above [17,18] require the application of relatively large samples and the use of detectors which do not decompose the substance, since the lower limit of the sensitivity of the reagent varies from 20 to 100 μg.

Janak [109] employed a similar attachment to the pen recorder for the crystal-chemical identification of substances isolated on a preparative scale. High-boiling compounds, separated in a capillary column at 280°C, were condensed on a thin glass sheet moving at a distance of 1–2 mm from the chromatograph outlet and cooled from inside. These compounds formed bands 3–4 mm wide with characteristic microcrystals. The author investigated the crystals under the microscope and described a method for the preparation of coloured complexes by carrying out the reaction with samples of the substances isolated weighing 10^{-2} μg and having a volume of 10^{-5} ml. Janak [109] investigated the crystals of 15 aromatic hydrocarbons (naphthalene, anthracene, phenanthrene, fluorene, benzopyrene, and other polycyclic hydrocarbon derivatives) as well as certain oxygen-, nitrogen-, and sulphur-containing compounds. Sublimatograms and a colour table of the complexes of the test compounds with tricyanoethylene are quoted.

IV. SCHEMES FOR THE CONSECUTIVE GROUP ANALYSIS OF HYDROCARBON MIXTURES

This section deals with examples of group analysis of hydrocarbon mixtures in which elimination and transformation methods are combined in a single scheme with chromatographic separation at each stage of the treatment.

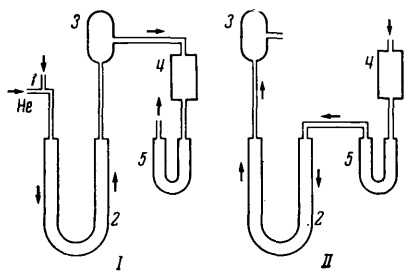


Figure 1. Schematic illustration of Martin's gas-chromatographic apparatus[32]: 1) injector; 2) analytical column; 3) katharometer; 4) absorber with $HgClO_4$; 5) trap.

Martin[32] developed a combined method for the analysis of petrol based on the elimination of substances of certain classes. The gas stream scheme is illustrated in Fig. 1. A column with $\beta\beta'$-oxydipropionitrile retained aromatic hydrocarbons. Naphthenes, paraffins, and olefins were recorded by the detector in the form of a single peak (*A* in Fig. 2). Beyond the katharometer, the sample passed through an absorber with mercury) perchlorate (Fig. 1, position I). Olefins were absorbed in the absorber and paraffins and naphthenes were collected in a cooled trap. By altering the direction of the carrier gas stream (Fig. 1, position II), aromatic hydrocarbons were initially eluted from the column in the form of a single peak *B* and then the trap was warmed and saturated hydrocarbons (peak *C* in Fig. 2) were recorded.

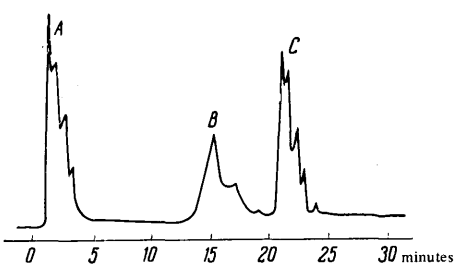


Figure 2. Chromatogram of a hydrocarbon mixture[32]: *A*) naphthenes + paraffins + olefins; *B*) aromatic hydrocarbons; *C*) paraffins + naphthenes.

Albert[33] employed a similar scheme for the analysis of petrol having supplemented it by the elimination of straight-chain paraffins and the interpretation of each peak. Aromatic hydrocarbons were initially retained on a column with *NN'*-bis-(2-cyanoethyl)formamide as the stationary phase and the remaining hydrocarbons were eluted from the column, detected by the katharometer, passed through an absorber with mercury perchlorate and a molecular sieve, and were collected in a trap. After heating the trap, the stream of gas was directed to the column and branched-chain paraffins were separated and detected. Finally the absorber with the molecular sieve was heated for 15 min at 400°C and the gas stream was again switched to the column, whereupon the desorbed straight-chain paraffins were identified component by component.

The most complete method of group analysis of hydrocarbon mixtures by a continuous procedure was proposed by Rowan[23]. The apparatus is illustrated schematically in Fig. 3. As in the examples described previously, its principle involves the switching of the gas stream and chromatography of the sample collected in the trap after preliminary separation. Steps of the following types were employed: retention of straight-chain hydrocarbons on a 5 Å molecular sieve, absorption of olefins by mercury perchlorate, hydrogenation of aromatic hydrocarbons and olefins, hydrogenation of olefins alone, and dehydrogenation of six-membered naphthenes. The analytical scheme illustrated in Fig. 4 combines the operations enumerated above and makes it possible to select the required sequence of steps.

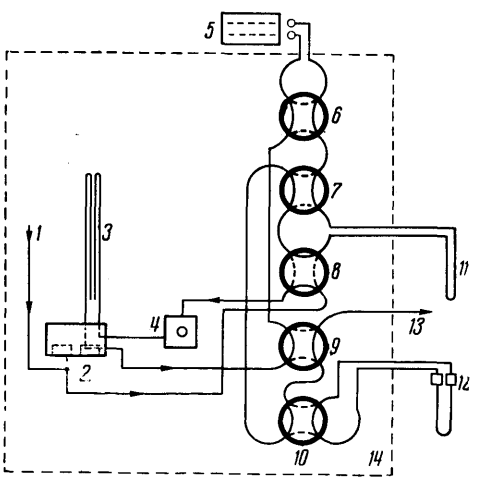


Figure 3. Schematic illustration of Rowan's gas-chromatographic apparatus[23]: 1) carrier gas supply line; 2) katharometer; 3) analytical column; 4) injector; 5) furnace; 6)–10) four-way taps; 11) cooled trap; 12) absorber with sulphuric acid or 5 Å molecular sieve; 13) outlet; 14) chromatograph thermostat.

Reactors with sulphuric acid, mercury perchlorate, and a molecular sieve can be replaced and interchanged. Sulphuric acid was deposited on glass fibre and the absorber temperature was maintained at 54°C. The reactor with mercury perchlorate was constructed by Coulson's method[110]. The water evolved in the reaction with olefins was absorbed by a layer of a 4 Å molecular sieve. Adsorption was carried out with the aid of a 5 Å

molecular sieve at 93° and 165°C, depending on the boiling point range of the fraction analysed. Palladium on asbestos (5% Pt) was employed as the catalyst for the hydrogenation of olefins at room temperature, while the hydrogenation of aromatic hydrocarbons and the dehydrogenation of naphthenes at 299°C were carried out on the platinum–alumina catalyst proposed by Keulemans and Voge[97].

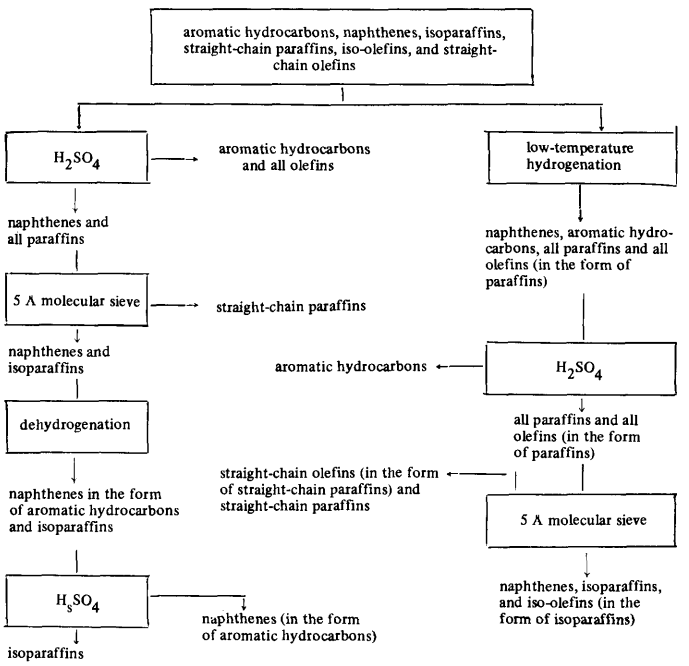


Figure 4. Analytical scheme for the assignment of gas-chromatographic peaks to different classes of hydrocarbons[23].

Fig. 3 shows the taps in the position where the sample, having passed column *3*, proceeds via taps *9* and *6* into the catalytic furnace *5* and is then collected in trap *11* after passing through taps *6* and *7*. After trap *11* has been heated and tap *8* switched over, the concentrated hydrocarbons are again directed to column *3*. The changes which have occurred are recorded by the katharometer and the specimen is returned to the trap via an absorber with the appropriate reagent.

The method was tested on artificial mixtures of hydrocarbons of different classes but without cyclopentane derivatives, acetylenes, and conjugated dienes and also on technical petrol in which the fraction of aromatic components predominated.

Methods for continuous group analysis of hydrocarbons were developed also for exhaust gases[31] and atmospheric contaminants[28].

A scheme of group analysis[24], involving the identification of olefins, conjugated dienes, acetylenes, and straight-chain paraffins, has been developed for hydrocarbons present in gases in microconcentrations.

Hoff and Feit[111,112] described a consecutive functional analysis of a vapour–gas mixture of hydrocarbons and oxygen-containing compounds by the method of "syringe reactions".

Several schemes for the type analysis of liquid hydrocarbon mixtures have been proposed recently. They require an apparatus modified by the introduction of additional valves, by-pass systems, and chambers with various heating devices. In their practical application these schemes differ from those already described by the fact that provision is made for the heating of the taps, in order to prevent adsorption, and cooled traps for the collection of samples for repeated analysis are eliminated. This made the new methods more accurate and faster.

Robinson et al.[37] described a system comprising the two capillary columns and a device which divides the sample into two equal portions. One portion passes through the empty column into the detector, giving rise to a signal corresponding to the size of the entire sample, while the other passes in succession through a column with *NN'*-bis-(2-cyanoethyl)formamide, where aromatic hydrocarbons are retained reversibly, and a reactor with mercury perchlorate for the irreversible retention of olefins. Thus the second chromatogram shows only paraffins and naphthenes. The back-flushing device makes it possible to switch the direction of the stream and to transfer aromatic hydrocarbons from the *NN'*-bis-(2-cyanoethyl)-formamide column to the detector. The third chromatogram shows aromatic hydrocarbons. The olefin content is calculated from the difference between the peak areas on the three chromatograms.

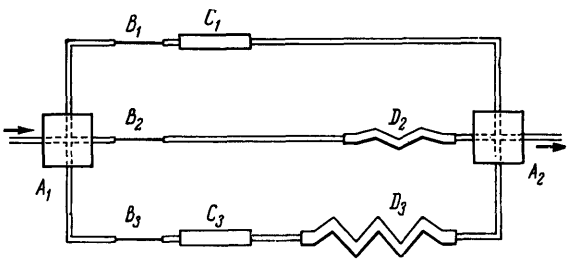


Figure 5. Schematic illustration of the analyser[35]: A_1 and A_2—four-way connecting sleeves; E_1, E_2, and B_3—capillary connections; C_1—absorber with $HgClO_4$.$HClO_4$; C_3—absorber with $HgSO_4.H_2SO_4$; D_2 and D_3 flow retarding devices.

A scheme for analysis in which the sample is divided into three streams (Fig. 5) was proposed by Soulages and Briewa[35]. One part of the sample passes to the detector without hindrance, olefins are subtracted from another in a reactor with H_2SO_4, and olefins and aromatic hydrocarbons in the third are retained in a reactor with $HgClO_4$. In order to avoid the superposition of peaks, capillary sections were fitted in the path of each sample in order to regulate the flow rates. The subdivision of the sample into three [equal] parts was adjusted by introducing pure heptane and comparing the areas of the three peaks. The time required to apply the methods described[35,37] is 5–15 min.

McTaggart and Luke[36] introduced an improvement into type analysis by introducing an additional stage involving the separation of paraffins, naphthenes, and olefins on the

basis of the number of carbon atoms. The method provides for the introduction of two liquid samples of equal size. In the first cycle of the analysis aromatic hydrocarbons are retained on a packed column with *NN'*-bis-(2-cyanoethyl)formamide. The remaining hydrocarbons pass through a reactor with a platinum catalyst (Pt/Al_2O_3), where olefins are reduced quantitatively to the corresponding paraffins and naphthenes. Together with the paraffins and naphthenes present in the initial mixture, they pass to a column with a 13X molecular sieve treated with alkali and are separated on the basis of the number of carbon atoms according to the method of Brunnock and Luke[113]. In the same analytical cycle the aromatic hydrocarbons retained on the column are flushed out with the aid of the back-flushing device and recorded by the detector in the form of a single peak. In the second analytical cycle aromatic hydrocarbons and olefins are retained irreversibly in a reactor with mercury perchlorate and paraffins and naphthenes are separated on the basis of the number of carbon atoms.

By subtracting the areas of the corresponding peaks obtained on the first and second chromatograms after separation on the molecular sieve, the content of olefins is calculated and the results of analysis are produced in the following form:

Paraffins	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	C_{11}
Naphthenes	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	C_{11}
Olefins	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	C_{11}
Cyclo-olefins	C_1	C_5	C_6	C_7	C_8	C_9	C_{10}	C_{11}
Aromatic hydrocarbons	Sum							

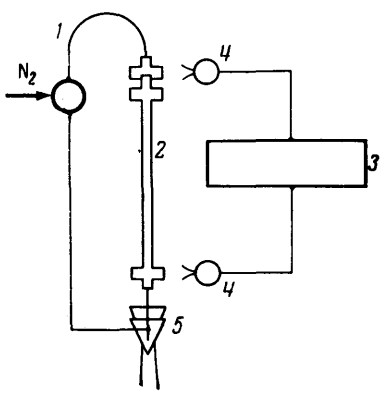


Figure 6. Trap and device for the reintroduction of sample[116]: 1) flexible tube; 2) trap; 3) heater; 4) clamp; 5) injector.

Comparison of reaction chromatographic methods[35-37] with the FIA type method[114] (adsorption separation on a silica gel column in the presence of an indicator, which dyes the boundaries between the following bands: paraffins and naphthenes–olefins–aromatic hydrocarbons), which is widely used for hydrocarbon mixtures, demonstrated a satisfactory agreement between the results. Reaction chromatographic methods require much less time and are applicable to highly coloured specimens.

The analytical methods described have been applied to hydrocarbon fractions boiling up to 180–220°C. An analytical scheme incorporating hydrogenation, molecular sieve analysis, partition and displacement chromatography, and spectroscopic research techniques has been proposed[115] for hydrocarbons boiling in the range 160 to 250°C.

In the present section of the review it is useful to consider the very promising method of "multidimensional chromatography"[116]. In contrast to the methods described earlier, in this case type analysis is not based on the application of chemical reactions but on a consecutive separation on columns with stationary phases of different polarity. While the components are eluted from the nonpolar phase in order of increasing boiling points, the order of their appearance after separation on the polar phase depends mainly on their polarity. The following series in terms of increasing polarity holds for hydrocarbons: paraffins < aliphatic olefins + naphthenes < < aliphatic dienes + cyclo-olefins < acetylenes < cyclodienes < aromatic hydrocarbons.

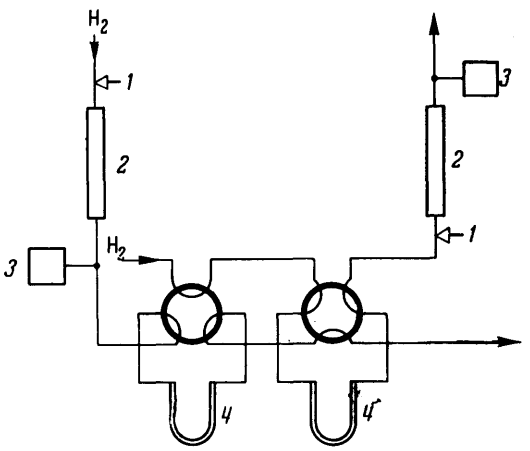


Figure 7. Schematic illustration of the universal two-dimensional chromatograph[116]: 1) injector; 2) analytical column; 3) detector; 4) trap.

Boer[116], who employed successfully the method of multidimensional chromatography for the analysis of complex hydrocarbon mixtures, regards it as "quantitative trapping of the required fraction after separation on the first column and its introduction into the second column". The method can be applied in continuous and discontinuous schemes. The first case has the advantage of the possibility of employing any standard chromatograph. It is only necessary to connect to it via a three-wave tap a heated trap (duration of heating to 250°C 10–15 s) and a device for the reintroduction of the sample (Fig. 6). A universal apparatus for continuous analysis is illustrated in Fig. 7. It consists of two chromatographs connected by a system comprising two traps and several devices, which can be switched in different directions, for the reintroduction of the sample and for back-flushing. Stream dividers are placed before flame-ionisation detectors. One part of the fraction is detected, while the other is directed to further analysis.

Boer[116] describes also more complex schemes with four columns and three traps and a specific example of the analysis of a petroleum fraction. The petroleum fraction was introduced into the first column with a polar phase (cyanoethylsucrose). Saturated hydrocarbons together with benzene and toluene were detected, the results integrated, and the substances collected in trap *1*. The residual aromatic hydrocarbons were flushed out in the opposite direction, detected, the signals integrated, and the substances collected in trap *2*. The contents of trap *1* were introduced into a second column with a non-polar phase (SF-96) and divided, under the conditions of a programmed temperature, into 24 fractions, which were collected alternately in trap *3* and directed one at a time into a third column with a polar phase (picryl chloride). The contents of trap *2* were then introduced into a fourth column (SF-96) and chromatographed under isothermal conditions. The analysis yielded 86 peaks and the weight and molar percentages of isoparaffins, naphthenes, and aromatic hydrocarbons were determined for each group with identical numbers of carbon atoms.

The principles of multidimensional chromatography constitute the basis of a standard apparatus for the analysis of petroleum fractions[117,118]. During an analytical cycle lasting 2–3 h, it is possible to obtain the following data: the individual compounds present in the aromatic hydrocarbons and the distribution of straight-chain paraffins, isoparaffins, and naphthenes among groups corresponding to numbers of carbon atoms ranging from 5 to 12.

Analysis of pyrolytic petrol is more difficult owing to the presence of olefins and dienes. Boer[116] suggests that the specimen be separated on a non-polar phase into very narrow fractions, which are chromatographed in succession on a polar phase.

Attempts are now being made to develop a scheme for the standard analysis of industrial mixtures containing olefins[117].

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Institute of Synthetic Alcohols
and Organic Products,
Moscow

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Gas Chromatography of Organometallic Compounds of Groups I-IV of the Periodic System

V.A.Chernoplekova, V.M.Sakharov, and K.I.Sakodynskii

The development of the gas-chromatographic analysis of organometallic compounds of groups I-IV of the periodic system in the period 1960-1972 has been reviewed. The characteristic features of the gas-chromatographic analysis of organometallic compounds have been discussed. The use of reaction chromatography for the analysis of the organic compounds of the metals of groups I-IV has been examined. The bibliography contains 238 references.

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I. INTRODUCTION

The present review deals with the gas chromatography of organic compounds of the non-transition metals of groups I–IV. It should be noted that published data on the gas chromatography of the organic compounds of non-transition metals are not evenly distributed. There are almost no papers on the analysis of organic compounds of rubidium, caesium, barium, indium, or thallium, and few papers on the gas chromatography of organometallic compounds of groups I–III, apart from organomercury compounds[1,2]. The problems of the gas-chromatographic analysis of organometallic compounds of group IV have been examined in most detail[3,4].

As far as the analysis of the organic compounds of transition metals is concerned, the gas-chromatographic analysis of the organic compounds of most transition metals is still in the stage of initial development.

II. CHARACTERISTIC FEATURES OF THE GAS-CHROMATOGRAPHIC METHOD FOR THE ANALYSIS OF ORGANOMETALLIC COMPOUNDS

Organometallic compounds are generally highly reactive, many tending to undergo spontaneous ignition or oxidation by oxygen and hydrolysis by water. With the exception of some lower alkyl derivatives, these compounds are solids or liquids with boiling points in the range 200–450°; they are most frequently thermally unstable at temperatures close to the boiling point.

As a consequence of these characteristic features of the physicochemical properties and structure of organometallic compounds, the gas-chromatographic analysis exhibits various specific features.

Stationary phases and carriers. The gas chromatography of organometallic compounds most frequently involves gas-liquid chromatography. Gas-adsorption chromatography has found only limited application[5-7].

The high boiling point of most organometallic compounds makes it necessary to use high-temperature stationary phases, and the increased reactivity of organometallic compounds restricts the choice of materials considerably. Thus of the hundred or so sorbents used for the analysis of organometallic compounds, more than half have silicone stationary phases (the methylsilicones PMS, Se-30, E-301, MS-200, and Gi-7100; the phenylsilicones PFMS, FS, DC-550, DC-702, and OE-4011; the fluorosilicones SKTFT, QF-1, and SF-96, and the nitrylsilicone XF-1112). Much less extensive use is made of strongly polar stationary phases (nitrobenzene and 1,2,3-tris(2-cyanoethoxy)propane), phases of medium polarity (dibutyl phthalate, dinonyl phthalate, diethylene glycol succinate, and butane-1,4-diol succinate), or hydrocarbon phases (Apiezon). In the selection of the stationary phase it is necessary to take account of the possibility of decomposition of the organometallic compounds. In particular, alkyltin hydrides decompose on squalane, chlorosilanes on polyethylene glycol[8], and alkylmercury halides on tricresyl phosphate[9].

As a rule, the separation of organometallic compounds is carried out using sorbents with a low percentage of stationary phase (5–10%); this makes it possible to lower the working temperature and to prevent the thermal decomposition of the compounds being analysed, to decrease the time taken for the analysis, to increase the length of time for which the stationary phase can be used, and to extend the choice of stationary phases.

Organometallic compounds are polar or weakly polar compounds, and the most inert diatomite carriers are used for their analysis (celite 545, Chromosorb W, Silo-cel S-22, modified Inzer brick, and quartz sand (flusine) [sic][9]). The carriers have been modified by treatment with silanes[8] or alkali[10] to decrease their catalytic activity. The use of Fluoroplast carriers is of considerable interest.

Characteristic features of the operation of detectors, and quantitative measurements. The thermal conductivity detector has found the most extensive application in the analysis of organometallic compounds. At high filament temperatures, or when high concentrations of the organometallic compounds are used, however, partial decomposition of the compounds on the incandescent filaments of the catharometer takes place[8]. The metal, which is deposited in a highly dispersed state, and the tarry residues bring about a decrease in sensitivity and an increase in the noise level. In these cases it

is best to use a catharometer with glazed filaments, and to dry the carrier gas thoroughly, in order to avoid the deposition of hydrolysis products in the detector.

A density meter has been used successfully by a number of authors[8,11,12] in the analysis of organometallic compounds. The calibration of a detector of this type is simple.

In early work on the gas chromatography of organic compounds of silicon and tin[13,14], the separated compounds were oxidised to water and carbon dioxide, with subsequent conversion of the water into hydrogen (detected by Green's method[15]).

When a flame-ionisation detector is used, the combustion of the organometallic compounds leads to the formation of the metal oxides, which accumulate on the electrodes; these oxides are insulators, and they alter the electrical characteristics of the detector[8]. A number of authors[8,16] have observed inversion of the peaks of organometallic compounds when a flame-ionisation detector is used. The detection of organosilicon compounds in the form of negative peaks by using a mixture of hydrogen and small quantities of methane as carrier gas has been proposed[16,17]. Organic compounds are then recorded as positive peaks, with a lower sensitivity.

The most reliable results have been obtained using a flame-ionisation detector with both electrodes in the vertical position and a hydrogen burner with a nozzle of small cross-section, since a decrease in the diameter of the nozzle of the burner increases the rate of flow of gas and decreases the proportion of oxidation products[18].

The sensitivity of the flame-ionisation detector towards organometallic compounds is less than its sensitivity towards organic compounds[8,18], and a sharp decrease in sensitivity takes place with increase in the relative proportion of metal in the molecule of the organometallic compound[19]. In spite of the above difficulties, the flame-ionisation detector has been used for the analysis of organic compounds of tin, silicon, lead, and mercury[8,10,18-23].

In the analysis of micro-quantities of organometallic compounds in various media it is possible to use highly-sensitive selective detectors—electron-capture, thermo-ionic, flame-emission, coulometric, and flame-photometric. The electron-capture detector has an increased sensitivity with respect to organomercury and organolead compounds and is often used for their analysis[24-31] including their determination in the biosphere (air[31], water[26,29], and soil[28]). The electron-capture detector has also been used in the analysis of alkyltin and alkylgermanium halides[32]. Traces of organometallic compounds containing halogen atoms have been identified by comparing the signals from thermo-ionic halogen and flame-ionisation detectors[33]. The sensitivity of electron-capture or thermo-ionic detectors is greater than that of flame-ionisation detectors by a factor of several hundreds or even thousands[24].

In the analysis of organosilicon compounds, use has been made of a specific "silicone" detector, based on a combination of flame-emission and atomic-absorption detectors[34].

Different methods of quantitative analysis are used in the analysis of organometallic compounds; the internal-standard method is most frequently employed, and the absolute-calibration method is used less frequently. Wurst[12] has analysed the errors in the quantitative determination of organosilicon compounds. The results are typical of the quantitative analysis of other types of organometallic compound. The mean relative error usually does not exceed 7% if the component is present in quantities of 1–2%. The error is appreciably smaller (3%) at higher concentrations of the component. At very low concentrations of the order of 0.1–0.001%, the mean error reaches 10–12%.[19] In quantitative calculations it is necessary to take account of the possibility of mutual transformations ['scrambling'] of the organometallic compounds being analysed[35].

Methods of introducing the specimens. In the case of reactive organometallic compounds which tend to ignite spontaneously, the specimens are introduced in an inert atmosphere. Fig. 1*A* gives a diagram of the so-called three-needle method for the introduction of specimens[36]. When the nitrogen outlet is closed, the specimen is forced into the syringe.

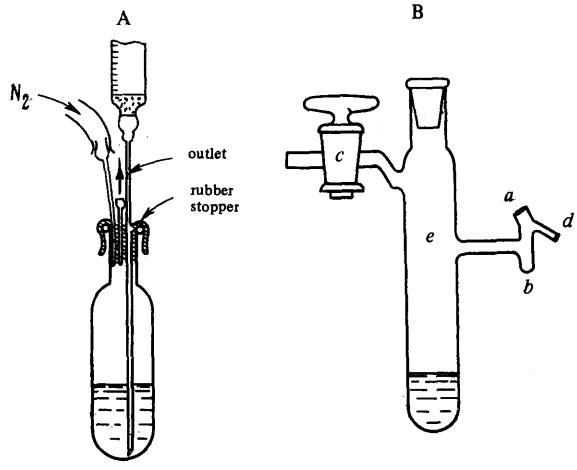


Figure 1. Apparatus for working with unstable liquids.

The specimen can be introduced into the chromatograph[37] directly from the sampler (*e*) (Fig. 1*B*). For this purpose, part of the specimen is poured into the cell (*b*). The needle of the micro-syringe is introduced through the stopper of the tube (*a*) and the syringe is flushed beforehand by passing a stream of dry nitrogen through the tap (*c*). The needle is then lowered into the liquid and the syringe is filled. For the introduction of the specimen into the chromatograph, the needle of the syringe is introduced into the tube (*d*), the end of which is closed by a stopper; when the latter is punctured, the specimen passes to the volatiliser of the chromatograph.

In some cases the introduction of specimens can be carried out by means of syringes previously flushed with an inert gas and carrying on the ends of their needles a self-sealing covering[38].

The drying of the carrier gas is most frequently carried out with phosphorus(V) oxide and molecular sieves. A method for the quantitative determination of the residual moisture in gases after drying has been published[39]. The sensitivity of the determination corresponded to 2×10^{-3} mg water in 1 litre of gas for a volume of specimen being analysed equal to 0.5 ml.

III. RELATIONSHIP BETWEEN THE STRUCTURE AND CHROMATOGRAPHIC BEHAVIOUR OF ORGANOMETALLIC COMPOUNDS

For the identification of organometallic compounds, use is made of the usual relationship between the retention and structure of organic compounds[40-42], but in a number of cases the behaviour of organometallic compounds is so unique that all the correlations must be rigorously verified. Sometimes it is more appropriate to relate the retentions of organometallic compounds not to the retention volumes of the normal paraffins, used as standards, but to the retentions of a series of organometallic homologues.

Wurst[43] put forward modified retention indices I_{Si}, in which the retentions are related to the dimethylsiloxane series

$$I_{Si} = y + m\frac{\lg V_{N(x)} - \lg V_{N(y)}}{\lg V_{N(y+m)} - \lg V_{N(\ )}}$$

where $V_{N(x)}$ is the retention volume of the substance being analysed, and $V_{N(y)}$ or $V_{N(y+m)}$ the retention volumes of the linear dimethylsiloxanes with y or $(y + m)$ silicon atoms.

An advantage of this system is that the substances belong to the same class, but a slight disadvantage is the difficulty of carrying out a comparison with the retentions obtained on the basis of other standards.

One of the most important correlations between retention and structure is the relationship between the retention and the number of groups or atoms of the same type (analogous to the relationship between the logarithm of the retention volume and the number of methylene groups in homologous series of organic compounds). These relationships have been used to identify the products of the synthesis of mixed hydrides of silicon and germanium, which were obtained in small quantities and were present as mixtures in the reaction product[44].

Some authors have reported deviations from the linear dependence of the logarithm of the retention volume on the number of carbon atoms in series of organometallic compounds[45,46], and this must be taken into account in correlation calculations. The extended additivity scheme for the calculation of the retention volume has not been used. A retention volume calculation scheme, developed for the calculation of thermochemical quantities[47], has proved useful.

The additivity of the logarithm of the retention volume and the retention index has led to the development of a method of calculation for asymmetric compounds from the retention values for symmetric compounds[48-50]. The retention volumes for compounds of the type $R_2MR'_2$ were calculated from those of symmetric organometallic compounds of the type R_4M formed by silicon, germanium[48,49], and tin[50].

Retention volumes for compounds in which the two parameters change simultaneously (for example cyclosiloxanes containing two different siloxane groups in the ring) can be represented by means of nomograms[51] (Fig. 2).

IV. GAS CHROMATOGRAPHY OF ORGANOMETALLIC COMPOUNDS OF GROUPS II AND III

The gas-chromatographic analysis of organometallic compounds of the first group by the direct method is apparently impossible, because of the low volatility of these compounds. The reaction chromatography of organometallic compounds of the first group is examined in section VI.

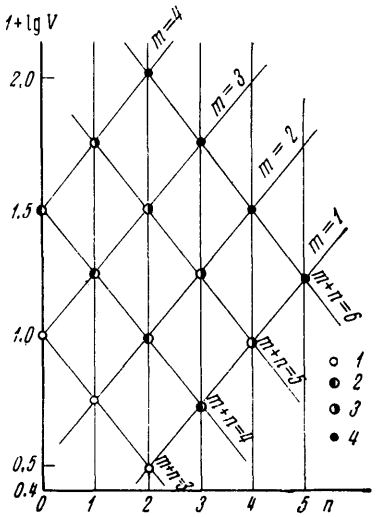


Figure 2. Dependence of the logarithm of the retention volumes of methylpropyldimethylcyclosiloxanes on n, where $n = 0-5$, $m = 0-5$, and $m + n = 3-6$. *1*) Cyclotrisiloxanes, *2*) cyclotetrasiloxanes, *3*) cyclopentasiloxanes; *4*) cyclohexasiloxanes.

Table 1.

Type of compound	Conditions of analysis	Detector	Notes	References
Et_nM, M—Be, B, Zn, Al, Sn, Pb	Glass column. 1 m x 4 mm, sorbent: Chromosorb W + paraffin and diphenylamine (85:15), 73°, 143°	Catharometer		38
RHgX	Steel column. 0.19 m x 3 mm, sorbent shimalite + 25% diethylene glycol succinate, butane-1,4-diol succinate, silicone DC-550, 170-200°	Flame-ionisation		23, 27, 60, 63,
RHgX	Steel column. 2 m x 3 mm, glass column, 2.75 m x 4 mm, carrier Chromosorb W + 5% polyethylene glycol succinate, flusine + 1.5% polyethylene glycol, 140-150°	Catharometer, electron-capture		25, 26, 64, 65
RHgX, X=Cl, Br, $OOCCH_3$, SO_4, OH	Column 1-3 m x 3 mm, sorbent Chromosorb W + 10% 13 stationary phases, 120-200°	Electron-capture	Decomposition of RHgX on tricresyl phosphate and butanediol succinate	9

Group II

The chief conditions for the analysis of the ethyl derivatives of beryllium, zinc, boron, and aluminium, and other organometallic compounds of groups II–IV are systematised in Tables 1–3, the data in which give a fairly clear picture of the characteristic features of the gas-chromatographic analysis of this group of compounds.

Organomagnesium and organocalcium compounds have been analysed by reaction chromatography (see section VI).

Organomercury compounds. The high toxicity of organomercury compounds makes it necessary to develop effective methods for the analysis of the biosphere for contamination by these compounds.

Table 2.

Type of compound	Conditions of analysis: stationary phase, temperature	Detector	References
Alkylsilanes	Polyphenylsilicone oil, polyethylene glycol M 1500, 100–175°; silicones SE-30, QF-1, XF-1112	Catharometer	50, 77, 98–100
Chlorosilanes, methylchlorosilanes	Nitrobenzene, 25°; mixture of diethyl phthalate and silicone oil, 104°; benzophenone, 52°; transformer oil, 106°; liquid paraffin and insulating oil, 50–60°; PFMS-4, DS-703, 40°; phthalates, phosphates, silicones	Catharometer, flame-ionisation	101–112
Ethylchlorosilanes	Silicone MS-0150, 90°. PFMS-4, FS-16, 50–100°	Ditto	113–116
Phenylchlorosilanes	Apiezon L + bentone-34 (1 : 1); E-302 120°; silicone MFSD-3, PFMS-4; silicone rubber; Lucopren G-1000, temperature programming; SKTFT-50, 120°; SE-30, temperature programming	»	12, 91, 92, 117–121
Alkylchlorosilanes	Dinonyl phthalate, 40°; nitrobenzene, 40°; PFMS-4, FS-16, 151°; fluorosilicone 169, 160°	»	122–126
Linear and cyclic siloxanes	Silicone DS-703, 125°; Lucopren M, 150–195°; copolymer of diphenylsiloxane and dimethylsiloxane, temperature programming; Apiezon L; PFMS-100, temperature programming; SKTFT-50°; PDMS 80 M, 160–190°; silicone OE-4011, 60°; SKTFT-50, 190–250°; dimethylsiloxane with carboranylene or diphenyl oxide groups, 235–260°	»	40, 127–146
Alkoxysilanes	Silicone G-7100, 175–180°; E-301, 150–180°; SKTFT-50, 175°, 235°		147–150

Methods have been developed for determining organomercury compounds in food[52–56], water and aqueous solutions[26–29], and soil[28,57], based on the extraction of the organomercury compounds from the natural materials, followed by gas-chromatographic analysis.

The selectivity of 16 stationary phases for the separation of alkyl and aryl compounds of mercury has been studied, and it has been established that the best separation is achieved on diethylene glycol succinate and butane-1,4-diol succinate at 160°.[25]

Methods have been developed for the analysis of methylmercury and phenylmercury compounds in various mixtures[28,58–62] (in phenylmercury acetate[28] and in specimens containing sulphides[58]).

For the identification of a number of organomercury compounds, Kitamura and coworkers[62] used a combination of thin-layer and gas chromatography. The conditions for the analysis of compounds of the type RHgX are given in Table 1.

Determination of the retention times of compounds of the type RHgX, with different substituents, on the stationary phases diethylene glycol succinate and butane-1,4-diol succinate established that the retention time is independent of the nature of the substituent X, and is determined by the length of the alkyl radical[24,25]. The fact that the measured retention times of different compounds of the type RHgX are identical is due to the decomposition of these compounds in the volatiliser with the formation of dimethylmercury[66]. The decomposition products were determined by means of flame-ionisation and electron-capture detectors (Fig. 3).

Highly-sensitive selective electron-capture and emission detectors[67] have been used for the determination of micro-quantities of organomercury compounds. A method has been developed for the determination of nanogram quantities of a dialkylmercury by means of a flame-ionisation detector and an MAS-50 detector; this has been proposed for the determination of organomercury compounds in river water[29].

Table 3.

Type of compound	Conditions of analysis	Detector	References
Alkylstannanes, alkyldistannanes, tin hydrides	Column 2 m × 6 mm, sorbent Chromosorb W + 20% polyethylene glycol 20 M, silicone E-301, 200	Catharometer	50
Alkyl- and arylhalogenostannanes	Column 1 m × 4 mm, sorbent celite 545 + 5% silicone oil MS-200, 180°, 200°	Flame-ionisation	185
Mono-, di-, and trihalogenostannanes	Column 2 m × 4 mm, sorbent Sterchamol + 15% silicone OE-4011, 160–180°	Catharometer	186
	Column 2 m × 3 mm, sorbent Sterchamol + 5% polyethylene glycol 20 M, silicone OE-4011, 160–170°	"	35, 187
Dibromodialkylstannanes	Capillary column 2.5 m × 0.3 mm, coated with polyethylene glycol 20 M, 200°	Flame-ionisation	188

The minimal measurable quantity of methylmercury chlorides for the optimal conditions on a column containing butane-1,4-diol succinate is 10^{-12} g when an electron-capture detector is used[24]. A method for the analysis of compounds of the type RHgX is given in section VI.

The chromatographic and biological aspects of the behaviour of organomercury compounds[2], and the analysis of organomercury compounds by photometric, spectroscopic, and chromatographic (paper, thin-layer, and gas chromatography) methods[1] have been reviewed.

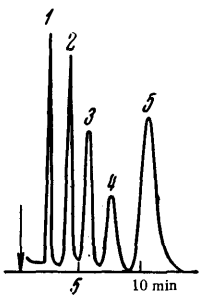


Figure 3. Chromatogram of alkylmercury chlorides. 25% diethylene glycol succinate (4 m × 4 mm), 160°, nitrogen flow rate 80 ml min^{-1}. *1*) Methylmercury chloride; *2*) ethylmercury chloride; *3*) n-butylmercury chloride; *4*) n-pentylmercury chloride; *5*) methylethylmercury chloride.

Group III

The gas chromatography of boron compounds has been carried out chiefly in the analysis of inorganic compounds, for example boron hydrides, borazoles, boranates, and derivatives of boric acid[68–77].

Organoaluminium and organogallium compounds have been analysed by gas chromatography as the ethyl derivatives[37,38]. It should be noted, however, that organoaluminium compounds are usually analysed by reaction chromatography (see section VI).

V. GAS CHROMATOGRAPHY OF ORGANOMETALLIC COMPOUNDS OF GROUP IV

1. Organosilicon Compounds

Study of reaction mechanisms and the composition of reaction products. The redistribution of radicals in a number of organometallic compounds often produces a wide range of components with similar structures, the study of which would be difficult by any method other than gas chromatography. Pollard[11,78] and Phillips[48] made extensive studies of the redistribution of tetra-alkyl derivatives of the group IV elements, including silicon (Fig. 4). These studies were subsequently continued[79,80].

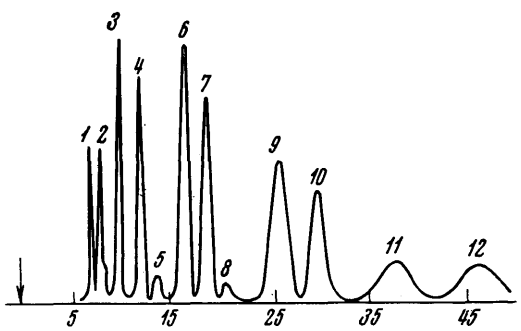


Figure 4. Chromatogram of the products of radical redistribution between $(n\text{-}C_3H_7)_4Si$ and Et_4Ge: *1*) Et_4Si, *2*) Et_4Ge + Et_3GeCl, *3*) $Et_3Si(n\text{-}Pr)$, *4*) $Et_3Ge(n\text{-}Pr)$, *5*) $Et_2(n\text{-}Pr)SiCl$, *6*) $Et_2Si(n\text{-}Pr)_2$, *7*) $Et_2Ge(n\text{-}Pr)$, *8*) $Et(n\text{-}Pr)_2GeCl$, *9*) $EtSi(n\text{-}Pr)_3$, *10*) $EtGe(n\text{-}Pr)_3$, *11*) $(n\text{-}Pr)_4Si$, *12*) $(n\text{-}Pr)_4Ge$.

The redistribution of alkoxy-groups or methyl groups with alkoxy-groups between silicon and phosphorus atoms or silicon and tin atoms takes place with difficulty[79]. Gas chromatography has been used in this case for the analysis of small quantities of products of the redistribution of the radicals, which would be extremely difficult to study by other methods. The analysis was carried out with 25% silicone oil on celite at 100–150°.

Redistribution in sterically hindered tetra-alkylsilanes containing isopropyl and isobutyl groups has been studied[80]. The deviation of the distribution of the reaction products from the statistical distribution is particularly marked for radicals with a long hydrocarbon chain. The specific retention volumes of the redistribution products were measured on E-301 methylsilicone (15% on Sil-o-cel) at 150–200°. A remarkable feature is the nonlinearity of the graphs giving the dependence of the logarithm of the retention on the number of carbon atoms (or number of radicals of the same type) for isopropylsilane, n-pentylsilane, and isobutylsilanes; this is apparently due to the steric influence of the atoms in the molecules of the substances being separated. Deviation from linearity has been observed in other analogous cases[81]. The exchange of alkyl radicals between heterocyclic organosilicon compounds has been studied[82,83]; in the first of the works cited, the reaction between hexamethylcyclotrisilathiane and nonamethylcyclotrisilazane was investigated, and two new cyclosilathiazanes were studied. The redistribution of methyl and ethyl radicals in alkylcyclotrisilazanes has been studied[84]. The reaction products were separated by gas chromatography with a detector sensitive towards nitrogen. The compounds were identified more accurately by NMR.

The products of various other reactions have been studied by gas chromatography[85-93]; the composition of the products of the reaction of methyl chloride with a copper–silicon alloy has been determined[86]; and the products of the reaction of hexamethyldisilazane and polymethylchlorosilane have been studied[87].

It has been proved by gas-liquid chromatography that in the presence of iron pentacarbonyl, ethers are split by triethylsilane with the formation of triethylalkoxysilane and hydrocarbon. The alkoxysilanes were analysed on a column containing 5% silicone elastomer on Chromosorb R at 134°.[88] The composition of acyl compounds of silicon has been studied by gas-chromatographic analysis of the reaction products[89].

The products of the catalysed formation of 1,1-dimethylcyclopentasilane were studied by Nametkin and coworkers[90] by gas chromatography. The electrophilic chlorination of phenylchlorosilanes and benzylchlorosilanes has been studied[91,92]. It has been established that the ratio of the quantities of meta- and para-isomers obtained depends on the type of catalyst.

Gas chromatography has been used to study the equilibrium constants of reactions of methylphenoxysilanes and phenylchlorosilanes[93]. Polymethylsiloxane was used as stationary phase, at 230°.

The products of the pyrolysis of phenyldimethylsilane[94,95], aryltrimethylsilanes[19], and tetramethylsilanes[96] have been studied, and the products of the thermal decomposition of tetra-ethoxysilanes have been analysed[97]. The conditions for the analysis of organosilicon compounds of various types are given in Table 2.

Organosilicon compounds containing hetero-atoms in the molecule. Bortnikov[5-7] used gas-liquid and gas-adsorption chromatography to separate organometallic compounds of group IV containing a bond between two silicon, germanium, or tin heteroatoms, and to separate heterocyclic compounds containing silicon and germanium atoms. Various thermodynamic parameters of *cis*- and *trans*-isomers of 1,2-bis(trimethylsilyl)-substituted ethylenes and their germanium analogues have been determined on graphitised carbon black and Apiezon L[5].

The processes of intermolecular sorbate–sorbent interaction in solution and on the surface of an adsorbent have been studied for organometallic compounds of the type $Et_3M\text{–}M'Et_3$ (M and M′ = Si, Ge, and Sn). The separation of these compounds on columns containing Apiezon L, 20 M polyethylene glycol, and graphitised carbon black has been studied. The absolute retention volumes and differential heats of adsorption and dissolution were measured, and the electronic polarisabilities of the compounds were determined[6].

It has been found that graphitised carbon black is a

promising sorbent for the separation of various organometallic compounds, containing two or three hetero-atoms, and sterically hindered silicon-containing ortho- and para-isomers of phenol derivatives[7].

The analysis of impurities is necessary in the study of the purity of monomeric materials in the production of highly pure substances for semiconductor technology (silicon dioxide, silicon carbide) and in the production of polymers.

A number of authors[151-155] have determined impurities in monomeric organosilicon compounds. Traces of dimethyl ether, ethanol, and benzene have been determined in triethoxysilane, trichlorosilane, and methyl chloride[152].

Impurities in methyltrichlorosilane—the starting material for the production of single crystals of silicon—have been identified as chlorides and oxide chlorides of boron and phosphorus on a column containing fluorosilicone oil 169 and DS-701 silicone oil[153]. Impurities in the form of derivatives of aluminium, iron, magnesium, and calcium were absorbed by the stationary phase, and the concentration of metals was reduced below 10^{-6}–10^{-7} wt.%.

Impurities in trichlorosilane were determined on a glass column containing silica gel modified with trimethylchlorosilane[33]. The carrier gas was dried thoroughly, and the concentration of moisture was 5×10^{-4} mole %. Methanol, ethanol, propane, 2-methylpropane, butane, ethyl chloride, silicon tetrachloride, and methylchlorosilane were identified by comparing the signals from thermo-ionic and flame-ionisation detectors. The sensitivity of the determination was $1 \times 10^{-4} - 5 \times 10^{-2}$ mole %.

The vat residues remaining after the fractional distillation of commercial dimethyldichlorosilane were found to contain traces of ethylchlorosilane, tetramethyldichlorosilane, and hexamethyldichlorotrisiloxane. The individual components were separated by preparative chromatography[154]. Traces of cross-linking agents in the raw material for the production of silicone rubbers have been determined[136]. Traces of bis(dialkylsilyl)arenes, arylsilanes, and halogenobenzenes in the products of the manufacture of monomers for silicone rubbers were identified on a column containing 5% of an arylene siloxane polymer with the formula $[-SiMe_2-Ar-SiMe_2-O-]_n$, where Ar = $-C_6H_4-$ and $-C_6H_4-O-C_6H_4-$, at 141–146°.[155] Traces of water have been determined in polyorganosiloxanes and the carrier gas in the analysis of readily hydrolysed organosilicon compounds[39,156].

Preparative chromatography of organosilicon compounds. Preparative chromatography has been used to separate the components of complex reaction mixtures[153,154,157,158]. The method has also been used to separate a number of deuteriated organosilicon compounds. Deuteriated methylethoxysilanes were separated on a column (7 m × 33 mm) containing 20% dinonyl phthalate on Inzenskii brick at 95°. 1,4-Bisdeuteriomethyltetrasiloxane was isolated on a column (4.8 m × 17 mm) containing 20% SKTFT-50 on S-22 celite at 154°.[157]

Chromatographically pure chlorosiloxanes have been isolated on a column (4.8 m × 17 mm) containing as sorbent 20% SKTFT-50 on S-22 celite at 150–190° in order to convert them into methylated and deuteriated derivatives for mass-spectrometric studies[158]. The purity of the products was 99.2%.

Isomeric high-boiling organosilicon compounds have been isolated by micro-preparative chromatography[159]. The use of a highly efficient trap packed with filter material increased the efficiency of recovery to 95%.

Turkel'taub[160,161] examined the possibility of the preparative isolation of high-boiling organosilicon compounds (b.p. 500–600°C) and proposed organosilicon stationary phases for preparative chromatography[162].

Determination of the physicochemical properties of organosilicon compounds. Gas-liquid chromatography can be used to solve such problems as the choice of separating agent for the extractive separation of mixtures of methylchlorosilanes[163], the determination of the solubility of nitrogen and oxygen in organosilicon liquids[164], and the study of the molecular weight distribution of polydimethylsiloxanes[132].

Gas chromatography has been used most widely for the determination of the saturated vapour pressures and boiling points of organosilicon compounds on the basis of their retention values on non-polar stationary phases[11,42].

2. Organogermanium Compounds

There are relatively few papers on the gas chromatography of organogermanium compounds[5,11,41,44,49,165-172]. Gas chromatography has been used for the first time for the analysis of silicon and germanium hydrides[44,165-167], for the separation of tetramethyl derivatives of germanium on a column containing Apiezon L at 60°,[99] and in the determination of the percentage composition of azeotropic mixtures of trimethylgermanium chloride and diethyl ether on a stationary phase of DS-550 methylsilicone at 70°.[168]

Gas chromatography has been used to study the redistribution of the radicals of tetra-alkyl derivatives of germanium[11], to determine the products of the alkylation of alkylchlorogermanes[170] and the electrophilic chlorination of alkylchlorogermanes[171], and to identify organogermanium compounds in the products of the exchange reaction of bis(triethyl)germylmercury with organotin halides[172].

The additivity method for the calculation of the retention times of unsymmetrical compounds from data on the retention of their symmetrical analogues has been applied for the first time for organogermanium and organosilicon compounds[48,49]. Organogermanium compounds were separated on a column containing squalane (2–13%) or a column containing a mixed phase consisting of 3% squalane and 3% phenylsilicone 702 at 100–150°.

Retention data have been published for a number of organogermanium compounds[41,48,49,125].

Gas-adsorption and gas-liquid chromatography have been used to separate the *cis*- and *trans*-isomers of 1,2-bis(trimethylgermyl)-substituted ethylenes and their silicon analogues[5] on graphitised carbon black and Apiezon L. The retention volumes and the heats of adsorption and dissolution have been measured for these compounds.

3. Organotin Compounds

The first papers on the gas-chromatographic analysis of organotin compounds appeared in 1960–1961[13,99,173-175].

Tetramethyl-derivatives of tin, germanium, silicon, and lead were analysed by Pollard[99] on a column containing Apiezon L at 60°. The preparation and chromatographic analysis of perfluorovinyltin derivatives have been described[173,174]. Matsuda[175] used gas chromatography for the analysis of tin derivatives of the type R_nSnX_{4-n}, where R represents radicals from methyl to pentyl, and X = chlorine, bromine, or iodine. The stationary phase was DS-550 silicone, the temperature 170°, and the column length 3 m.

Study of reaction mechanisms and the composition of reaction products. Gas chromatography has been used to identify the products of the reaction of tetra-alkyl compounds of tin with tin tetrachloride and tetrabromide[176] and the redistribution of the radicals of tetra-alkyl derivatives of group IV metals[11] (Fig. 5).

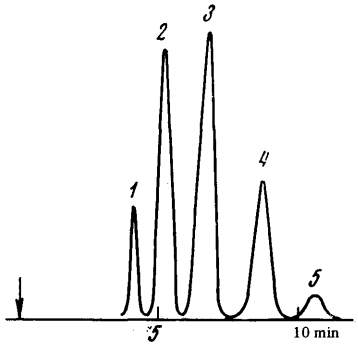


Figure 5. Chromatogram of the products of radical redistribution between $(n\text{-Pr})_4Sn$ and $(n\text{-Bu})_4Sn$: *1*) $(n\text{-Pr})_4Sn$, *2*) $(n\text{-Pr})_3Sn(n\text{-Bu})$, *3*) $(n\text{-Pr})_2Sn(n\text{-Bu})_2$, *4*) $n\text{-PrSn}(n\text{-Bu})_3$, *5*) $(n\text{-Bu})_4Sn$.

The products of the redistribution of the radicals were identified on the basis of the linear dependence of the logarithms of the retention volumes on the number of carbon atoms or the number of substituents of the same type.

Advantages of gas chromatography as a method for studying the redistribution of the radicals include not only the simple and reliable identification and effective separation of the reaction products but also the possibility of carrying out the reaction with extremely small quantities of material (0.002–0.01 mole).[11] The separation of the reaction products was carried out on a 2 m column containing 15% squalane E-301 on S-22 Sil-o-cel. The temperature of the analysis varied in the range 100–250°, depending on the composition of the reaction products.

The use of gas chromatography made it possible to study the exchange of methyl and alkoxy groups between tin and silicon atoms or between tin and phosphorus atoms[77], the hydrostannation of unsaturated compounds, and the reactions of trimethylstannane[75,177].

Gas chromatography has been used to identify the products of many reactions: the redistribution of radicals between alkyltin trichlorides and compounds of the type $RSnR'_3$,[178] the radiolysis of methyl and ethyl derivatives of tin[179], the reactions of tetra-alkyl derivatives of tin and germanium under the influence of ^{60}Co γ-radiation[32], the thermal degradation of tetrabutyltin[180], the reactions of tetra-alkyl-derivatives of tin with boron trichloride[181] and of metallic tin with alkyl halides[182], the reactions of bis(trifluoromethyl)diazomethane with organotin compounds[183], and the photolysis of tetramethylstannane[184].

The analysis of organotin compounds of different types is represented in Table 3.

Retention values have been published for various organotin compounds[11,41,45,50,189].

Putnam[45] measured the retention indices of 14 organotin compounds of the type R_4Sn on three stationary phases[45]. The retention indices of the organotin compounds are slightly larger for polar stationary phases, particularly in the case of unsaturated radicals. The ratio of the retention index to the molecular weight for a polar column shows a correlation with the refractive index of the organotin compound. The dependence of the retention indices on the number of carbon atoms, the molar refraction, and the boiling points has been given, and can be used for the approximate estimation of these quantities for organotin compounds.

With temperature programming, the indices of organotin compounds on a non-polar phase depend little on the rate of heating and change in the same sense as the molar refractions of these compounds[189].

Some deviations from the linear dependence of the logarithm of the retention volume on the number of carbon atoms in homologous series of organotin compounds have been noted[11,45,46]; these must be taken into account in the calculation of retention values by the additivity scheme. These deviations are apparently due to the mutual screening of the tin atom and the methyl groups from the interaction with the molecules of the stationary phase[46].

Preparative chromatography has not yet found extensive application for the separation of organotin compounds. Only the preparative purification of tetramethyltin and tetraethyltin on a column (13 m × 25 mm) containing 18% polyethylene glycol 400 has been described. A 10 ml specimen was purified in 40 min. The concentration of impurities in the product was 10^{-3}%.[190,191]

The determination of impurities in tetrabutyltin and the analysis of alkyltin halides by reaction chromatography are examined in section VI.

Some additional information on spectroscopic and chromatographic methods in the analytical chemistry of organotin compounds is given in two reviews[3,4].

4. Organolead Compounds

Organolead compounds are widely used as additives in motor fuel. Before the development and comprehensive application of chromatographic methods, the analysis of alkyl compounds of lead in petrol involved the determination of the total lead content. In the earliest work[99,192,193] on the gas-chromatographic analysis of organolead compounds, the components separated on the chromatographic column were detected by means of a spectrophotometer or catharometer.

Lovelock and Zlatkis[194] were the first to use for this purpose an electron-capture detector, the sensitivity of which towards organic compounds of lead is several times greater than its sensitivity towards hydrocarbons. The use of an electron-capture detector helped to solve the problems of the identification of complex mixtures.

In addition to organic compounds of lead, petrol always contains alkyl halides which prevent the successful separation of the mixture. An additional column containing as sorbent 20% polyethylene glycol, saturated with silver nitrate, on Chromosorb W treated with 8% potassium hydroxide, was proposed for the separation of alkyl halides[195]. This column was placed after a separating column containing 15% methylsilicone SE-30 on Chromosorb W. 1,2,3-Tris(2-cyanoethoxy)propane[196] and Apiezon L[197] have also been used for the separation of alkyl compounds of lead.

Soulages[10,198] developed a method for the simultaneous

determination of alkyl compounds of lead and alkyl halides in petrol. The analysis involved the separation of the alkyl compounds of lead and the alkyl halides from the hydrocarbons of the petrol on a sorbent consisting of 10% polyethylene glycol 400 on Chromosorb P and hydrogenolysis of the alkyl-lead compounds and alkyl halides at 140° on nickel deposited on Chromosorb P. The reduction products methane and ethane were separated on a column containing active carbon, modified with 3% vaseline at 70°. An electron-capture detector was used.

The above method was used in subsequent work by the same author for the determination of five methylethyl derivatives of lead and alkyl halides in petrol[10]. The separation was carried out on a stationary phase consisting of 1,2,3-tris(2-cyanoethoxy)propane on Chromosorb P, treated with 1% potassium hydroxide at 80°.

The identification of mixtures of organolead compounds is made difficult by the lack of pure specimens of the alkyl compounds of lead for the calibration of the detectors. Soulages[22] put forward a simple method of identification with thermal-conductivity and flame-ionisation detectors. The catharometer recorded the alkyl compounds of lead and the alkyl halides separated on the chromatographic column. Simultaneously, the flame-ionisation detector recorded, in the form of methane and ethane, the products after hydrogenolysis. This method was used to identify a mixture of tetramethyl-, tetraethyl-, trimethylethyl-, dimethylethyl-, and methyltriethyl-lead, dichloroethane, dibromoethane, and toluene, separated on a column containing 10% polyethylene glycol 400 and 1% tetrakis(2-hydroxypropyl)ethylenediamine on Chromosorb W.

In the determination of alkyl compounds of lead in aromatic petrols, an additional column containing Apiezon L was used for the separation of the aromatic hydrocarbons. The alkyl compounds of lead were separated on a sorbent consisting of 10% 1,2,3-tris(2-cyanoethoxy)propane on silanised Chromosorb W at 75° or 85°.[199] The chromatogram of the separated products is shown in Fig. 6.

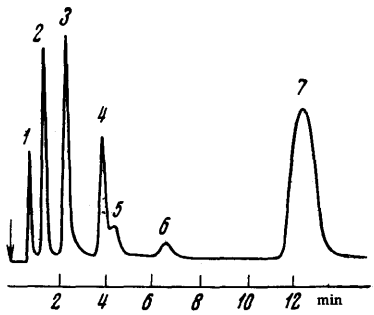


Figure 6. Chromatogram of alkyl compounds of lead, 10% 1,2,3-tris(2-cyanoethoxy)propane (4 m × 3 mm), 85°, nitrogen flow rate 30 ml min^{-1}. *1*) Me_4Pb, *2*) Me_3PbEt, *3*) Me_2PbEt_2, *4*) $MePbEt$, *5*) $C_2H_4Cl_2$, *6*) Et_4Pb, *7*) $C_2H_4Br_2$.

A combination of gas chromatography and atomic-absorption spectroscopy has been used for the quantitative determination of organolead compounds in petrols[200]. The quantitative analysis does not require the calculation of correction coefficients.

All lead compounds are highly toxic, and their concentration in the surrounding atmosphere must be strictly controlled. In the analysis of organolead compounds in air, the problems of concentration of the specimen immediately arise. The use of Yanak's method[201] of concentration, involving the passage of air through an absorbing column filled with the sorbent used in the separating column, has been proposed[31]. Air was forced by means of a pump through a column (8 cm × 1 mm) containing 10% silicone SE-52 on Chromosorb P for 10–15 min. After the concentration, the column was heated rapidly, and the lead compounds were introduced into the chromatographic column, on which the separation was carried out at 80°. An equation was put forward for calculating the concentration of alkyl compounds of lead in air.

VI. REACTION CHROMATOGRAPHY OF ORGANOMETALLIC COMPOUNDS OF GROUPS I–IV

Many organometallic compounds of groups I–IV have a low volatility and are unstable towards atmospheric moisture and oxygen. It is difficult to analyse these compounds by classical methods of gas chromatography, so that in most cases it is not the organometallic compounds themselves, but their transformation products, which are analysed. The version of gas-chromatographic analysis in which chemical reactions are used to convert the substances into forms more convenient for analysis is called reaction chromatography. We shall subsequently use this term in the description of this type of work.

GROUP I

Reaction chromatography has been used for the analysis of organic compounds of lithium, sodium, and potassium, which in most cases are solid, almost non-volatile compounds. These are converted into more volatile compounds by hydrolysis. A system of two chromatographs[202] has been used for the analysis of solutions of vinyl-lithium in tetrahydrofuran. The specimen was hydrolysed on the first chromatograph in an additional column containing hexane-1,2,6-triol on Chromosorb. The ethylene liberated on hydrolysis was identified and determined quantitatively on a column containing 20% dodecyl phthalate on Chromosorb W at 75°. A second chromatograph, connected to the first, was used to determine the trace components present in the ethylene, such as acetylene and buta-1,3-diene, on a sorbent consisting of 20% dimethylsulpholane on brick.

Reaction chromatography has been used to study a number of reactions: the metallation of organic compounds with organopotassium compounds[203–205], the kinetics of the polymerisation of butadiene, isoprene, and styrene in the presence of an alkyl-lithium[206], the reaction of epichlorohydrin with butyl-lithium[207], and the products of the reaction of methylcyclopentane in the presence of benzylsodium[208].

GROUP II

Organomagnesium and organocalcium compounds, like the organic compounds of the group I metals, have a low volatility and are unstable to hydrolysis.

1. Organomagnesium Compounds

The conversion of these compounds into more volatile compounds by hydrolysis or by exchange with alkyltin and alkylsilicon halides has been proposed[209–213].

Reaction chromatography has been used for the first time for the analysis of ethylmagnesium iodide solutions, which were hydrolysed with phosphoric acid in a micro-reaction vessel. The gaseous products were introduced into the chromatographic column through a by-pass line and separated on a column with activated silica gel.

The concentration of solutions of partly decomposed Grignard reagents (*p*-t-butylphenylmagnesium bromide) was determined by double chromatographic analysis[210]. The quantity of aromatic hydrocarbon formed by the decomposition of the Grignard reagent was first determined by direct gas chromatography on a column containing polyethylene glycol. The solution being analysed was then hydrolysed with methanol, and the quantity of t-butylbenzene liberated was determined. The results from the two analyses were used to calculate the true concentration of Grignard reagent in the solution. This method for the analysis of aryl Grignard reagents was subsequently used in a study of the kinetics of the reaction of alk-1-enes with phenylmagnesium bromide[211].

Tributyltin chloride has been used as reagent in the analysis of vinylmagnesium chloride[212]. This reaction gave vinyltributyltin, which was separated from the reaction products on a column containing 20% phenylsilicone DS-550 with temperature programming from 120° to 210° at a rate of 15 deg min^{-1}. This method of analysis appears more promising, since the reaction mixture contains a smaller number of components. The reaction with dimethylphenylchlorosilane has been used for the analysis of methyl Grignard reagents[213]. The trimethylphenylsilane obtained was determined quantitatively by the internal-standard method.

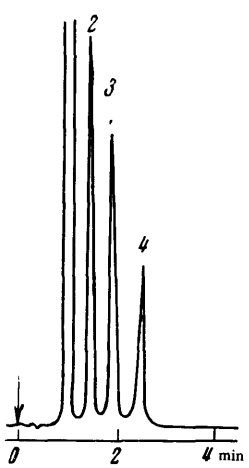


Figure 7. Chromatogram of the products of the hydrolysis of the complex of dioxan with phenylcalcium iodide: *1*) diethyl ether, *2*) benzene, *3*) toluene (standard), *4*) dioxan.

2. Organocalcium Compounds

Reaction chromatography has been used for the analysis of organocalcium compounds isolated for the first time in the individual state in the form of complexes with dioxan and amines[214]. The solution of the complex of dioxan and arylcalcium iodide in ether was decomposed with water. The CaI(OH) precipitate was separated by centrifuging. The aromatic hydrocarbon and dioxan obtained on hydrolysis were separated on a column containing 5% diethylene glycol succinate at 94° (Fig. 7). The quantitative determination of the aromatic hydrocarbon and dioxan was carried out by the internal-standard method. The method of analysis of organocalcium compounds by gas chromatography has made it possible to develop an optimal method for the preparation of diphenylcalcium.

3. Organomercury Compounds

There is only one published paper on the reaction chromatography of organomercury compounds; this describes the identification of a mixture of alkylmercury halides by means of the reactions with various sulphur-containing substances—sodium thiosulphate and metal sulphides—and metal powders[215]. The method involves double chromatography of the mixture being analysed; the separation is first carried out by the direct method, after which the solution being analysed is treated with various sulphur-containing compounds or passed through an additional column containing metal powder, and subjected to a second separation.

GROUP III

Reaction chromatography has been used chiefly for the analysis of organoaluminium compounds.

Organoaluminium Compounds

Organoaluminium compounds decompose readily under the influence of oxygen and water. The temperatures of the start of the thermal decomposition of these compounds are lower than the boiling points at atmospheric pressure.

Reaction chromatography has been used for the analysis of triethylaluminium, which is a catalyst for the preparation of polyethylene[216].

A solution of triethylaluminium in cyclohexane was evaporated in a stream of hydrogen and passed through a tube filled with 30% lauric acid on Sil-o-cel, connected to the chromatograph. The hydrolysis products were determined in two stages; ethane and butane were first determined on a column containing dibutyl phthalate, after which hydrogen and ethane were determined on a column containing silica gel.

In the analysis of triethylaluminium and tripropylaluminium, these compounds were hydrolysed with n-hexanol, diethylene glycol, and its mixture with aqueous sulphuric acid solution[217,218]. Hydrogen, methane, ethane propane, and butane were separated on dimethylsulpholane deposited on silica gel, and dinonyl phthalate on celite at 30°.

Palamarchuk[219] put forward a method for the analysis of triethylaluminium, in which the specimen was decomposed directly in the entry compartment of the reaction vessel. The specimen in an atmosphere of dry nitrogen was decomposed with diethylene glycol, and the hydrolysis products were transferred by the carrier gas into a separating column containing alumina. If the triethylaluminium contained impurities, for example diethylaluminium oxide, the alcohol and ethane liberated in its hydrolysis were separated on a column containing a mixed sorbent of 15% tricresyl phosphate on Polysorb and 10% squalane on Teflon.

Gas chromatography has been used for the analysis of the products of the reaction of α, ω-dienes with di-isobutyl-lithium hydride[220] and in the study of the kinetics of the reaction of alkyl compounds of metals with alkenes[221].

GROUP IV

Reaction chromatography has been used in the analysis of organosilicon and organotin compounds.

1. Organosilicon Compounds

Reaction chromatography has found extensive application in the structural analysis of organosilicon compounds. This method was developed by Franc and coworkers[222-227]. The method involves a number of reactions with BF_3, BCl_3, H_2SO_4, HNO_3, HI, Zn, NaOH, and KOH in a special reaction vessel (Fig. 8) to determine the structure of the organosilicon compounds and to detect functional groups. In the reaction with BF_3, the organosilicon compounds are split at the siloxane bonds, halogen and hydrogen are replaced by fluorine, and the phenyl radical is split off as benzene[225,227]. In hot concentrated sulphuric acid, alkyl-, aryl-, chloroalkyl-, and chloroaryl-silanes are split with the formation of hydrocarbons and alkyl halides[223,226,227]. Hydrogen iodide splits alkoxy-compounds with the formation of alkyl iodides[223,227]. Si–H and Si–Si bonds are split by potassium hydroxide solution with the formation of hydrogen. The reaction products are analysed by gas-liquid chromatography and paper chromatography[227].

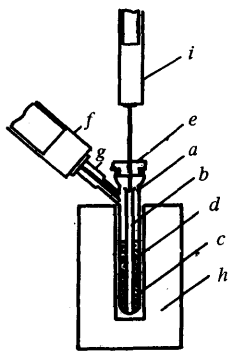


Figure 8. Glass reaction vessel for carrying out decompositions before application to the chromatographic column: *a*) glass vessel, *b*) glass tube, *c*) layer of calcium fluoride, *d*) layer of porous material (Risorb) [sic], *e*) silicone rubber stopper, *f*) 10 ml syringe, *g*) silicone rubber tube, *h*) copper block, *i*) 1 ml syringe.

A method of reaction thermal analysis has been developed, which makes it possible to determine the nature of a functional group and to establish the structure of a molecule on the basis of the reaction between the substance being studied and a suitable reagent, with temperature programming[225,226]. The method has been used to determine the structure of linear and cyclic polyorganosiloxanes by splitting these compounds with sulphuric acid. The relationship between the structure of the substance being studied and the temperature at which the separation of individual functional groups took place was examined. The thermograms of polyorganosiloxanes were given. A number of authors[228-230] have also used reaction chromatography for the analysis of organosilicon compounds. For the determination of Me_3Si-, $Me_2Si=$, and $MeSi\equiv$ groups in methylpolysiloxanes, it has been suggested that the polymer be depolymerised by the action of $2BF_3 .(C_2H_5)_2O$, with subsequent chromatographic analysis of the methylfluorosilanes produced[228]. The separation and quantitative analysis of a mixture of phenylmethyldichlorosilane, phenyltrichlorosilane, and silicon tetrachloride were carried out by converting them into the corresponding fluoro-derivatives on a column containing Na_2SiF_6.[229]

Gas chromatography has been used to study thermal processes taking place in polymers[231]. Pulse pyrolysis under chromatographic conditions has been used for the determination of vinyl groups in alkylcyclosiloxanes[232].

2. Organotin Compounds

Reaction chromatography has been used for the analysis of a mixture of alkyltin halides, which are thermally unstable and readily undergo radical redistribution[233,234].

Butyltin, octyltin, and phenyltin halides react with Grignard reagents with the formation of the more stable tetra-alkyl compounds, which have lower boiling points. For example, butyltin bromides are converted quantitatively into the butylmethyl analogues by the action of methylmagnesium bromide. The separation and quantitative determination of organotin compounds has been carried out on a column containing 20% methylsilicone SE-30 with temperature programming, from 50° to 270°.

Pyrolytic gas chromatography has been used for the determination of impurities in tetrabutyltin[235]. The substances separated on the chromatographic column were subjected to thermal decomposition, and the pyrolysis products in turn were separated on a column containing methylsilicone E-301 and recorded by means of a flame-ionisation detector. A number of impurities with general formula $(R_1)_nSn(R_2)_{4-n}$ (where R_1 and R_2 represent ethyl, methyl, butyl, or s-butyl) were identified.

VII. FUTURE DEVELOPMENTS IN THE GAS-CHROMATOGRAPHIC ANALYSIS OF ORGANOMETALLIC COMPOUNDS

The introduction of gas chromatography in the chemistry of organometallic compounds took place in the period 1960–1965. The gas chromatography of organometallic compounds can now be regarded as a sufficiently well-developed field of application of the method, but its possibilities have not yet been exhausted. We can expect an extension of the range of classes of organometallic compound analysed by gas chromatography, and also of the range of problems to be solved and versions of the chromatographic methods used.

Up to the present, almost no use has been made of capillary gas chromatography in the analysis of organometallic compounds; this is due to the adsorption of the organometallic compounds to be separated on the walls of the capillary, and the difficulty of detecting micro-quantities of organometallic compounds. When these difficulties have been eliminated, the use of capillary chromatography

for the separation of a large number of mixed isomeric compounds of several elements will appear particularly promising.

By analogy with the gas chromatography of organic compounds, we can expect the development of methods of combined chromatographic analysis (combination of gas and thin-layer, gas and liquid, and gas and paper chromatography).

Up to the present, only a few papers have been published on the use of highly sensitive selective detectors for organometallic compounds. An extension of the range of types of highly sensitive detector, and their more intensive use in the analysis of micro-components and the identification of organometallic compounds, appear probable.

The use of chromatography–mass spectrometry (for organomercury [63,236] and organosilicon [237] compounds) will apparently be extended after the elimination of a number of difficulties encountered at present, namely the non-availability of the mass spectra of many organometallic compounds, the complexity of the analysis of organometallic compounds under chromatography–mass spectrometric conditions, and the phenomena of instrument memory.

Gas chromatography is extensively used for the determination of the physicochemical characteristics of substances, the study of reaction mechanisms, and the study of catalytic processes [238].

We can expect the development of methods associated with the determination of physicochemical characteristics, and an extension of the types of reaction carried out under chromatographic conditions (catalytic reactions involving organometallic compounds).

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Karpov Physicochemical Scientific
Research Institute, Moscow